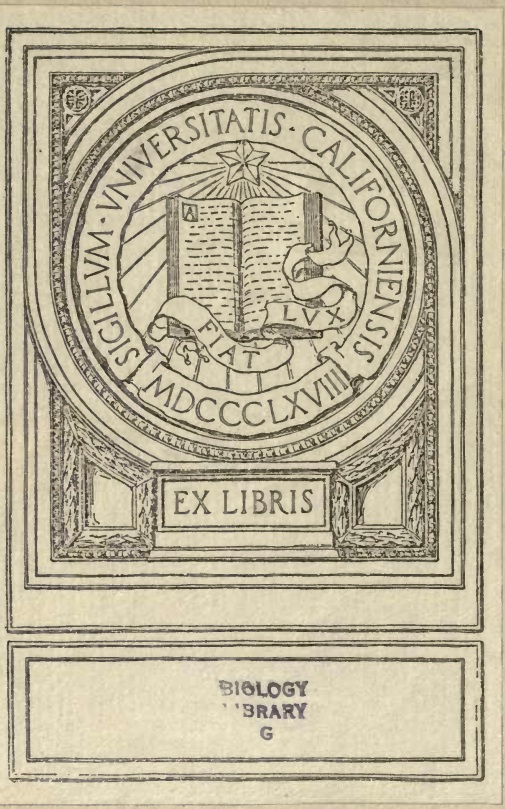

VITAMINS AND THE CHOICE OF FOOD

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BY

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PREFACE

AT the present time so much interest is taken in vitamins that a short account embodying the evidence in support of the need of these substances in nutrition will, it is felt, be of some service, and may in particular assist those who are responsible for the feeding of infants or for the selection of food in schools and other large communities.

The subject of accessory food-factors (vitamins) has a special significance, as it marks the entry of biochemical research into the problems of health and growth. Chemical formulæ as yet play no part. The small quantity in which these factors occur in the food-stuffs makes the isolation of the chemically pure substances from the complex chemical mixture, as it exists in nature, a very difficult problem. While the chemical nature of these substances is unknown, for the purposes of nutrition and health the investigator must carry on his work with the undetermined quantity which is present in a given food. It is known that some food-stuffs contain, and others do not contain, vitamins; and that faults in the diet are the cause of several diseases and of much ill-health.

Three lectures on vitamins were given by Dr. R. H. A. Plimmer at the Marischal College, Aberdeen, in the summer of 1920. Further lectures were given to suit the needs of special audiences, and numerous requests were received for a written account suitable for the general reader. This short summary has therefore been written in the hope that it may fulfil this purpose.

Prof. Gowland Hopkins's conception of unknown indispensable food-substances was first formulated in an address delivered to the Society of Public Analysts in

November 1906 (*The Analyst*, 1906, XXXI. p. 395), but his full account did not appear till 1912 (*Journal of Physiology*, 1912, XLIV. p. 423). Most of the papers on vitamins by British investigators have been published in the *Biochemical Journal*; others have appeared in the *Journal of Hygiene*, the *Proceedings of the Royal Society*, the *Lancet*, *British Medical Journal* and other medical periodicals. The researches of Osborne and Mendel and of McCollum and Davis, which led to the recognition of the A- and B-vitamins as two distinct entities, were published in the *Journal of Biological Chemistry* (Baltimore) from 1912 onwards. This journal publishes a large amount of scientific work by many authors upon vitamins and the quality of protein. Much of the early literature on the disease beri-beri appeared in German and Dutch publications, and is reviewed in E. B. Vedder's book *Beri-beri* (1913). Amongst papers in English on beri-beri may be mentioned the studies of Fraser and Stanton, in the collected papers of the Institute of Medical Research in the Federated Malay States. Valuable papers by Vedder and other investigators of beri-beri have appeared in the Philippine *Journal of Science* from 1910 onwards. The work of Goldberger on pellagra is contained in the Public Health Reports of the United States Public Health Service, from 1914 onwards. Wilson's paper on the diet factor in pellagra is in the *Journal of Hygiene*, July 1921.

Report No. 38 of the Medical Research Committee, 1920, gives a summary for the scientific worker of the whole subject of accessory food-factors, and contains lists of references to the original papers. *Studies in Deficiency Disease*, 1921, by Lt.-Col. R. McCarrison, I.M.S., contains an account of recent experimental work upon vitamins, and points out the way in which this information may be applied to the prevention of many chronic conditions of ill-health not usually ascribed to dietetic errors. The book is intended for the medical profession. Dr. A. F.

Hess's book on *Scurvy, Past and Present* (J. B. Lippincott Co.), 1920, is, again, for medical readers, and contains a detailed study of this disease.

We are greatly indebted to Prof. J. A. MacWilliam, F.R.S., Prof. Matthew Hay, and Dr. Thomas Fraser, D.S.O.,C.B.E., for their kindness in reading the manuscript and for many helpful suggestions. We also thank those investigators who have kindly allowed us to make use of their illustrations.

V. G. PLIMMER.

R. H. A. PLIMMER.

December, 1921.

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CHAPTER I

INTRODUCTION

A SUFFICIENT quantity of good and suitable food is the body's first need. Proper housing, fresh air and exercise play their part in maintaining health, but without good food they avail little. Famine, war and poverty interfere at times with man's normal food-supply, and his health suffers. Far more serious is the daily use of improper food; it insidiously undermines the constitution. A good diet must satisfy all the nutritional requirements of the body, but the amount of food needed varies under different conditions of life, and the kind is largely controlled by local circumstances. Generally a variety of food-stuffs is available, and if the diet consists of a few well-chosen natural foods of both vegetable and animal origin it will meet all the demands of the body. Under the conditions of modern civilisation a well-mixed and varied diet may be palatable and apparently sustaining, but if continued for a long time it may prove to be inadequate because it fails to supply everything that is wanted. A mixed diet of fresh meat, milk, butter, eggs, fruits, vegetables and wholemeal bread, such as our grandparents ate, supplied all that is necessary, but this food is now largely replaced by canned meat, sterilised milk, margarine, egg substitutes; bottled, tinned and dried fruits, vegetables and milk; white bread and other highly milled cereals. The effect of preservatives and refining processes has been to

destroy what may be called the vital substances in the food, substances as important as the actual food material itself.

The Composition and Function of Food.

The natural diet of man and animals contains certain substances every one of which is essential for the maintenance of life and health. These substances belong to the following groups :

(1) Proteins.
(2) Carbohydrates. } Known as the Proximal Principles.
(3) Fats.
(4) Salts.
(5) Water.
(6) Fat-soluble A-Vitamin.
(7) Water-soluble B-Vitamin. } Also called the Accessory Food Factors.
(8) Water-soluble C-Vitamin.

Except the vitamins, the relative proportions in which these various groups are present in the food is determined by chemical analysis. In fact, the relative proportions of protein, carbohydrate, fat, salts and water are the only data generally considered in judging the food-value of any diet. It is not possible as yet to determine the quantity of vitamins in the food. The following analyses [1] show the wide differences in the composition of various foods :—

Food-stuff.	Protein.	Carbo-hydrate.	Fat.	Salts.	Water.
Meat : beef, hindquarter .	16·6	—	29·86	0·82	50·8
Milk	3·3	4·8	3·6	0·7	87·6
Egg, boiled . . .	12·3	—	11·26	1·1	73·7
Fish, cod	15·7	—	0·1	1·1	70·3
Bread, white . . .	7·0	48·3	0·7	1·1	42·9
Cabbage	1·4	4·5	0·1	0·6	92·6
Potato, boiled . . .	1·5	19·9	0·02	0·9	77·2
Orange	0·8	8·8	0·1	0·5	87·0
Margarine	0·2	—	84·8	2·0	13·0

[1] The composition of common foods is given in *Analyses and Energy Values of Foods*, by R. H. A. Plimmer, 1921, from which these figures are taken.

The purpose of food is twofold; it is needed as a source of energy for the warmth and activities of the body, and to supply material for the growth of new tissues in the young animal and for maintenance in the adult, that is, for replacing substance lost to the body by wear and tear. Only a small amount of food is required for growth and maintenance by the adult, yet, as everyone knows, an adult eats more food than a rapidly growing little child. This is because the greater part of the food is used as a source of energy, and the body of the adult requires more energy, as it is larger to keep warm and heavier to move about. Even during the period of most rapid growth in the child, more food is used as fuel (energy) than for increasing the size of the body.

Metabolism.

The whole series of chemical interchanges undergone by substances in the body from the time they enter it as food till their removal as waste products is commonly referred to as metabolism. Anabolism includes all the processes which contribute to the building up of the living tissues; the reverse, or breaking down, processes are termed catabolism. These chemical changes are accompanied by an evolution of heat which is treated separately as the energy metabolism. The living organism conforms to the physical laws of conservation of mass and energy, so that any surplus output of material or energy over the intake can only be derived from a loss of body substance. The metabolism, both of energy and chemical material, can be expressed in the form of a balance sheet. The income is the amount of food taken into the body less the unabsorbed food passing out in the fæces. The expenditure of material is measured by the amount of carbon di-oxide gas breathed out by the lungs and by an estimation of the substances passed out in the urine, together with an allowance for the slight output of material through the skin. The heat given out during the chemical changes in the body is like the heat given out

by the burning of a coal fire in a grate. Both are processes of oxidation, that is of burning. All fuel consists of organic compounds. These compounds contain the element carbon; coal and the carbohydrates, fats and proteins are organic compounds. As the result of oxidation or burning, organic compounds, whether coal or food, combine with oxygen and are finally resolved into the gas carbon di-oxide, water and ash—the ash consists of the incombustible mineral salts in the fuel. The carbon di-oxide and some of the water formed by the combustion of food are breathed out by the lungs. Waste material from the tissues, incombustible (= ash) and incompletely burned material (= smoke) are excreted in watery solution by the kidneys. Certain constituents of the food are not digested and pass out in the fæces or stools.

The energy or heat which is liberated by the combustion of organic substances is used by the body for warmth and for movements of all kinds.

The Constituents of the Food.

The Carbohydrates.

Starch and sugar are the principal carbohydrates in the food.

Starch is the chief constituent of cereals, various kinds of flour, peas, haricot beans, potato, tapioca, sago, etc.

There are several kinds of sugar:

Cane sugar, or *sucrose*, from the beet, palm, maple, sugar-cane, etc.

Glucose, or *grape sugar*, the sugar in grapes and other fruits; also manufactured from starch and sold as a honey-like preparation.

Fructose, or *fruit sugar*, another kind of sugar in fruits.

Invert sugar, a mixture of glucose and fructose, in fruits, honey, jam, etc.

Lactose, or *milk sugar*, the natural sugar in milk; not sweet like other sugars to the taste.[1]

[1] Saccharin, although 550 times as sweet as cane sugar, is not chemically a sugar and has no food value.

Other carbohydrates are :

Glycogen, or animal starch, in small amounts in the muscles and liver of animals.

Malt and *Dextrin* are digestion products of starch. They can be prepared from barley.

Cellulose is present in all vegetable foods. It is not digestible and is passed out in the fæces.

All the carbohydrates, except cellulose, may be considered as identical for nutritional purposes. In whatever form the carbohydrate is eaten it is converted during digestion into a simple sugar, such as glucose. The carbohydrates function as fuel. A small reserve of carbohydrate is always retained in the body as glycogen, and any excess of carbohydrate is converted into fat and stored as a reserve of fuel.

Fats.

The edible fats, whether in the form of oil or solid fat, consist almost entirely of three fats—palmitin, stearin and olein. An oily fat contains more olein and a hard fat more palmitin and stearin. An oily fat is more easily assimilated than a hard fat. As a group the fats are practically alike, although there are further chemical differences which need not be discussed here.

Certain fats, such as butter, cod-liver oil, the fat of egg yolk, contain the fat-soluble A-vitamin, but leaving this vitamin out of consideration, the fats by themselves are of equal value in nutrition. The function of the fats is, like that of the carbohydrates, to supply heat and energy. Within certain limits fats and carbohydrates can be used alternatively in the diet. If all the carbohydrate in the food be replaced by fat, the fat is incompletely oxidised; in other words, carbohydrate burns more easily than fat, and for the complete combustion of fat in the body carbohydrate must be burned along with it. Mixed with carbohydrate it is as if fat burns with a clear flame, but if there is too little carbohydrate it burns smokily. The half-burned products of fat are poisonous to the body and

produce coma. This condition occurs in starvation, in diabetes and in children over-fed with fat, that is, in all cases in which fat is burned with an insufficient quantity of carbohydrate. Very little carbohydrate and a great deal of fat are eaten by the Eskimos, but they eat an abnormal amount of protein; in this case the protein acts like carbohydrate, assisting in the complete combustion of fat.

The body works more economically upon carbohydrate than upon fat, and severe work occasions greater fatigue if fat be the source of energy. If there is more fat than carbohydrate in the food, about 11 per cent. of the fat is wasted. The main difference between carbohydrate and fat is that carbohydrate is burned up quickly, while fat is a more sustaining fuel. The extreme cases of the athlete, who takes sugar whilst making great muscular effort, and the hibernating animal, which burns up slowly the fat stored in the tissues, may be contrasted.

Fats can be built up in the body from the carbohydrates in the food (p. 5), and some recent feeding experiments on rats indicate that fat as such can be omitted from the diet if the A-vitamin be supplied in a specially prepared fat-free form. The special value of fats in nutrition thus depends on the A-vitamin associated with them, and not on variations in their chemical composition.

Proteins.

Animal tissues consist for the most part of nitrogenous substances or albuminoids, which have received the name protein from the Greek word πρωτεύω, meaning "I am the first," that is the most important.

Proteins during digestion are converted into simpler compounds, the amino acids, which differ greatly among themselves. The number of amino acids is large; about eighteen to twenty have so far been recognised, and different amounts of them are contained in different proteins. We can thus speak of the quality of protein, but not of the quality of carbohydrate or fat. The quality of protein is of such vital significance in

nutrition that the subject is considered in a separate chapter.

Protein enters into the intimate structure of the living matter or protoplasm of the tissues, and from protein are probably derived some of the special glandular secretions, which control and co-ordinate the vital processes of the body.

Like carbohydrate and fat, protein is burned as a source of energy, but for this purpose it is wasteful. Theoretically there is no reason why protein could not be used to replace both carbohydrate and fat in the food as a source of energy, but from a practical point of view carbohydrate is a cheaper food than protein, and such a large quantity of protein as would then be required is not suitable to the digestion.

The Energy or Heat Value of the Food.

The energy value of fuel or food is measured in Calories. A Calorie is the amount of heat required to raise the temperature of 1 kilo. of water 1° C. Every combustible substance can be burned in a special apparatus called a calorimeter (= a heat-measurer), and the heat given out on complete combustion measured. Food burned in the body does not give quite such high values as when burned in the calorimeter, partly because cellulose, which is not burned in the body, is present, and partly because proteins are not completely oxidised, a certain proportion of their carbon being excreted as urea in the urine. The physiological Calorie values of food are generally reckoned as:

1 gram of protein gives	4·1	Calories
1 „ „ fat gives	9·3	„
1 „ „ carbohydrate gives	4·1	„

The Energy Output of Man

Man and animals can be put into another form of calorimeter, and the heat given out by them under different

conditions can be measured. In these experiments the subject is generally placed in the apparatus for a definite and short period of time. The amount of heat given out when the body is at absolute rest and without food, a state approximated during sleep, is known as the basal metabolism. The extra output of heat under different conditions as sitting, walking, riding a bicycle or at lower temperatures can also be measured. The average man of 11 stone (=70 kilos.) at rest gives out about 1 Calorie per hour per kilo. The figures are generally calculated in terms of Calories per 24 hours. The average quantities have been found to be:

Man's basal metabolism . .	1700 Calories.
Man without muscular work .	2700 ,,
Man with light muscular work .	3000 ,,
Man with moderate muscular work	3500 ,,
Man with hard muscular work .	4500 to 9000 or more.

Heavier men require a larger amount of energy, but the amount of energy per kilogram of body-weight is less than in the case of lighter men, because the area of the body-surface, and consequently the amount of heat lost from it, is relatively greater in smaller men.

The energy output of the individual varies according to occupation; it also varies according to sex, age, and the surrounding temperature. The average woman and child has a lower energy metabolism than man. In estimating the energy requirements of a family it is customary to use Lusk's coefficients: taking the man's requirement as 1; the woman requires only 0·83; boys over thirteen, 1·0; boy aged ten, 0·7; girl aged ten, 0·7; children under six, 0·5.

The science of calorimetry offers a convenient method of comparing the value of different diets without reference to the individual constituents. The Food (War) Committee of the Royal Society adopted the following scale of food requirements according to occupation:

Occupation.	*Food Requirements.*
Tailor . .	2750 Calories (approximate values).
Bookbinder .	3100 ,,
Shoemaker .	3150 ,,
Metal-worker .	3500 ,,
Carpenter .	3500 ,,
Painter . .	3600 ,,
Stonemason .	4850 ,,
Woodcutter .	5500 ,,

To supply the Calories for a man doing light work an average diet consisting of

100 grams of protein will give	410	Calories.
60 ,, ,, fat will give	558	,,
550 ,, ,, carbohydrate	2225	,,
Total	3193	,,

In general, the higher Calorie values required by individuals doing hard muscular work are supplied by increasing the amount of carbohydrate and fat. During the war, when the supply of protein foods was limited, the Royal Society Food Committee gave as a basis :

Protein . . .	70 grams	= 280	Calories.
Fat . . .	90 ,,	= 810	,,
Carbohydrate .	550 ,,	= 2200	,,
Total . .		3290	,,

The figures very closely approximate the former figures, but this diet differs in containing less protein and more fat.

The Protein Requirements.

The total energy value of the food is the sum of that of the three proximal principles. Theoretically these constituents can be varied at will so long as the total Calorie

value reaches the amount required for the particular occupation, but a definite minimal quantity of protein must always be present in the diet. Various investigators have attempted to fix this quantity. Atwater's figures are those generally accepted as the standard. Atwater calculated that 100 grams of protein were necessary for light work, 125 for medium, and 150 for hard work.

The protein figures refer to a mixture of animal and vegetable proteins. Less protein can be used if it be of animal origin; vegetable proteins have a lower value than animal proteins (see p. 110). The Calories are made up to the required amount by carbohydrate and fat in the proportion of about 10 to 1.

Salts and Water.

The salts in our food are the mineral constituents of meat, milk, cereals, plant tissues, etc., which form the residual ash after these food-stuffs are completely burned. The most common salts are the phosphates, sulphates, chlorides and carbonates of sodium, potassium, magnesium, calcium (= lime) and iron. The mineral salts have no fuel value, but they are essential constituents of the body and are contained in sufficient amount in an ordinary mixed diet. The only addition usually made is common salt (= sodium chloride) added according to individual taste, but this addition is not a necessity unless the food consists chiefly of cereals which are poor in sodium salts. Common salt is necessary for the formation of the hydrochloric acid in the gastric juice.

A diet composed largely of cereals is deficient in calcium salts, but they are most easily introduced in milk. To ensure a proper supply of all the salts it might be better to use a proper physiological mixture rather than a prepared table salt, which is deprived of some of the important constituents of the natural salt.

Water is contained in most foods and is partaken of according to natural desires.

Other Food Constituents.

Detailed analyses have shown that besides protein there are other nitrogenous substances: creatine, purine bases, etc., in animal tissues; amides, such as asparagine, and similar compounds of this type in vegetable tissues. Lipoids, such as lecithin, cholesterol and lipochrome pigments (the natural yellow colouring matter in butter, eggs and other fats) are contained in animal and plant tissues. All these compounds are present in natural foods in such small amounts that they are negligible with reference to their energy value, but they probably serve some definite physiological purpose.

Vitamins: Unidentified Constituents of the Food.

Physiologists and biochemists are ascertaining the function of all the known chemical constituents of the food. To study these questions feeding experiments on man and animals are carried out. It is, of course, impossible to use as protein natural products such as meat or milk which contain the other substances. The isolated or so-called "pure" protein must be used; also "pure" fat and "pure" carbohydrate. The preparation of pure foodstuffs involves a great deal of laborious chemical work as a preliminary to such feeding experiments.

The feeding of animals with pure protein, fat, carbohydrate, salts and water led to the discovery of some unknown substances which must be included in the food in order that life may be maintained. These substances are the vitamins or accessory food-factors. Altogether three distinct vitamins have been recognised:

Fat-soluble A-vitamin, present in certain fats, particularly cod-liver oil, butter, egg yolk, and also in green leaves.

Water-soluble B-vitamin, present in the seeds of plants, egg yolk, yeast and in many fruits and vegetables.

Water-soluble C-vitamin, in most juicy fruits and vegetables.

There is a common misconception that one vitamin is the equivalent of another, but this is not the case; there are three distinct vitamins, each one of which ranks as an essential food-substance and cannot be replaced by another vitamin. For practical purposes it is convenient to think of the three vitamins as (A) cod-liver oil, (B) the germ of cereals, (C) lemon-juice. These are three very different food-stuffs, and the vitamins which they contain are just as different.

The absence of these vitamins from the food leads to the so-called food deficiency diseases. Scurvy follows on a diet deficient in C-vitamin, beri-beri on a diet poor in B-vitamin, rickets is associated with a lack of A-vitamin. The curious disease, pellagra, is connected with the quality of the protein.

Although there is as yet no concrete chemical evidence of the existence of vitamins, experimental investigations show very definitely that health and growth depend on the presence of protein of good quality and of three accessory factors or vitamins in the food; that these vitamins are, generally speaking, very unstable to temperature and other influences; that they are very unevenly distributed in the various food-stuffs; that a sufficient quantity must be consumed every day; that, although they may exist in animal tissues, yet ultimately they are derived from plant food and cannot be formed in the animal organism.

Striking proof of the need and value of vitamins in the diet of animals is given by the practical agricultural experiments of Dr. M. J. Rowlands, carried out on a large scale. His animals, fed on a full vitamin containing diet, have not only grown unusually fast, but also have shown remarkable resistance to the ordinary diseases of animals. In competition at the Smithfield Fat Stock Show they gained the chief prizes. Further, he has shown that the full vitamin diet is a financially sound proposition.

CHAPTER II

BERI-BERI, THE RESULT OF HIGHLY MILLED CEREALS

BERI-BERI occurs mainly amongst the rice-eating people of the Malay States, Dutch Indies, Philippine Islands, China and Japan. The disease has been known in the Far East since the earliest times of which any record exists (2697 B.C.), but its prevalence has greatly increased since the introduction of machine-milling. Generally considered to be a tropical disease, beri-beri is by no means so limited in its distribution; it has been reported as far south as Sydney in Australia and as far north as Saghalien Island. The disease has originated in the Port of London in the crews of ships which have been in dock for several months; there have been cases in lunatic asylums in the United States and in Europe; in 1894 at the Richmond Asylum, Dublin, there were 150 cases and 23 deaths from beri-beri. In 1914 Surgeon-General Blue reported the existence of beri-beri in the county gaol at Elizabeth, New Jersey, U.S.A., and at one time all the inmates serving sentences of over sixty days had contracted the disease. In Newfoundland and Labrador there have been several seasonal epidemics of beri-beri. During the last war British troops in the Dardanelles and Mesopotamia and Annamite and Chinese troops in France suffered from beri-beri.

Symptoms.

The disease is characterised by severe nervous and heart symptoms and digestive troubles. In the " dry " form there is a paralysis and great wasting of the limbs; in the " wet " form there is a dropsical condition (œdema [1]) of the lower

[1] In œdema the tissues are distended and waterlogged with colourless fluid (lymph). Œdema of the limbs and trunk produces visible swelling, in which a " pit " or little hollow is temporarily produced by pressure.

limbs, in severe cases the trunk and arms are also affected. The departure from normal health is usually very gradual, beginning with such vague symptoms as loss of appetite and debility. As a practical test for the detection of incipient cases of beri-beri among the troops in the Dardanelles, Dr. (now Sir W. H.) Willcox made the men squat down, and those in whom the disease was beginning were unable to rise.

The symptoms do not appear in any definite sequence. Slight œdema of the feet and ankles is usually noticeable at an early stage, but may disappear again. The knee-jerk and other reflexes are increased at first but absent later. The early symptoms of nervous disorder are feelings of " pins and needles," or numbness of the feet and legs; the muscles, especially of the calves, are very tender to touch. The gait is unsteady, then becomes high-stepping, and finally the legs may be completely paralysed. The pulse is quick, palpitation is complained of; the heart is enlarged, especially on the right side, and may be displaced towards the right. Shortness of breath (dyspnœa) is sometimes very distressing. In a considerable number of cases the voice is lost.

From time to time stray cases exhibiting these symptoms are observed in Europe, and it is very likely that they are cases of beri-beri which have escaped diagnosis owing to the mistaken belief that it is a tropical disease peculiar to people living chiefly on rice.

Association with Diet.

During the period 1878 to 1885 it was recognised by certain medical men that this disease in the East was common among the poorer people living almost entirely upon a rice diet, and rare among the richer people whose food was much more varied. Wernich (1878) thought that the bulkiness of a rice diet interfered with the assimilation of food. Van Leent (1880) suggested that it might result from food containing too little fat and protein; the diet of the natives was usually very poor in fat and in nitrogenous foods such as meat, milk and eggs. It has since been shown that beri-beri can develop on a diet containing plenty of fat, so that an insufficiency of fat cannot be a contributory cause.

Takaki (1880–90), Medical Inspector-General of the Japanese Navy, believed that the prevalence of beri-beri in the Japanese Fleet was caused by nitrogen (*i. e.* pro-

tein) starvation. He made a comparative study of the general hygienic conditions of the Japanese and European navies and could find no essential difference except in the food; he concluded that the freedom from beri-beri in the European navies was connected with their higher protein diet. After a great deal of opposition he persuaded the Naval Authorities to make a change in the men's food. The quantity of rice was reduced, and in its place there was issued more meat, fish, flour, milk and vegetables, including beans; [1] the cost of the new ration was double that of the old. On the old ration 32 per cent. of the men in the Navy had suffered from beri-beri, and on one occasion some warships sent on active service to Chemulpo (1882) were obliged to return to port because the crews were unfit for battle, 195 out of 330 men being ill with beri-beri. The new ration was introduced in 1884, and in the first year the number of cases of beri-beri fell from 32 to 0·6 per cent. A minute investigation into the cause of these few cases showed that the disease was limited to a few prejudiced individuals who had persisted in eating rice only and refused the new food. Three years after the changed diet there was not a single case of beri-beri, although the personnel of the Navy had meanwhile been doubled.

Takaki's wonderful success in eliminating beri-beri from the Japanese Navy attracted much attention to his theory that nitrogen starvation was the cause. Numerous instances were now brought forward from other parts of the world of the development of this disease in people living on a good protein diet, and also of its non-appearance amongst people who had a ration even lower in nitrogen than the old Japanese Navy ration. The cause of the disease was therefore generally attributed to some infection. Nevertheless a better ration was continued in the Japanese Navy, but the Army ration still consisted chiefly

[1] The term *beans* will be used to denote the dried seeds of haricot and other varieties of beans, and does not include the green pods of French or runner beans.

of rice. The difference in the nutritive value of the two diets was remarkably demonstrated during the Russo-Japanese War in 1905; there was no beri-beri in the Navy, but 200,000 cases in the Army, which suffered from no other serious epidemic. The rations issued to the Navy and Army at the siege of Port Arthur may be considered as typical of the difference in the food of the two services:—

Japanese Navy.	*Japanese Army.*
1 lb. of meat.	5 oz. meat.
10 oz. of barley.	30 oz. of rice.
20 oz. of rice.	

It is now known that it was not the meat, but some constituent of the barley, which prevented beri-beri in the Navy. Experience in Japanese prisons proved the value of a mixed barley and rice ration without meat.

The prevention of beri-beri is easily effected in an army, navy, or prison by a change of diet, but it is impossible suddenly to reform the diet of the large populations in the East.

A new conception of the origin of beri-beri was given by Eijkman (1897), who noticed that some fowls kept at a prison in Java, of which he was medical officer, fell ill and suffered from a peculiar form of paralysis, which he called *Polyneuritis gallinarum*. No micro-organisms could be found which might be the cause of the disease. Eijkman discovered that these birds were fed upon the remains of the boiled rice from the prison. He therefore carried out feeding experiments upon birds with different kinds of rice. Some were fed upon the whole rice grain, some upon half-peeled rice, and some upon polished white rice. Only those birds which had been fed upon the polished rice for three or four weeks developed the disease; they were cured by being given either the whole grain or the half-peeled rice, or the polishings (= rice bran). The disease was produced by feeding with any sort of polished rice, whether fresh or old, cooked or raw, home-

grown or imported. None of the rice was infected with organisms of any sort. It was suggested that the monotony of the diet and consequent starvation might be the cause of the disease. This was disproved by the fact that birds on an equally monotonous diet of the half-peeled rice, or of the whole grain or potatoes, did not suffer; moreover, the symptoms of starvation were quite distinct from those of polyneuritis. Not only rice, but also sago, tapioca, or peeled barley as the exclusive diet were found by Eijkman to cause the disease.

Eijkman, with the help of his colleague Vorderman, put the results of these experiments to a practical test in 101 gaols in Java, containing altogether about a quarter of a million prisoners. The inmates of some prisons were given polished rice, of others half-peeled rice, and of still others a mixture of the two.

In the prisons receiving polished rice, 1 in 39 of the inmates had beri-beri; in the prisons receiving mixed rice, 1 in 416 had beri-beri; while in those receiving half-peeled rice, 1 in 10,000 had beri-beri.

The results with both birds and prisoners were thus very conclusive, but it could not definitely be proved that *Polyneuritis gallinarum* was the same as beri-beri. The evidence was not at that time considered sufficient to prove that a disease could be caused by the absence of some unknown substance in the food. With our present knowledge this evidence would be accepted. Grijns (1901) confirmed and extended Eijkman's observations, and showed that the disease could also be cured if " katjang idjo " [1] beans were added to the polished rice.

These Dutch observers also found that wheat germ, rye, barley, whole rice and potatoes lost their power of protecting from beri-beri if they were heated to 115° to 120° C. to sterilise them in order to eliminate micro-organisms as the cause of the disease.

A common criticism of Eijkman's experiments with birds was that they were carried out in an area in which beri-

[1] *Phaseolus radiatus*, a variety of haricot bean.

beri was prevalent, so that the birds might have become infected. Eijkman repeated his work in Holland, where beri-beri was unknown, on ducks and fowls, and confirmed his former results, so that the disease could not be due to a place infection.

Neither Eijkman nor other medical men understood at that time the real meaning of these discoveries, for it was difficult and almost impossible to dissociate micro-organisms from epidemic disease, either directly or indirectly through the action of toxins (poisons) produced by them. Much more work had to be done to establish the fact that such heavy mortality could be produced by a diet deficient in some unknown substance.

Fletcher and Gilmore Ellis, who had both believed firmly in the infectious origin of the disease, were convinced by their independent experiences with outbreaks of beri-beri in Malay and Singapore of the association of beri-beri with the use of white rice. A complete survey of the field was published by Braddon (1907) in his book *Causes and Prevention of Beri-beri*, and although he was wrong in attributing the cause to a poison in rice and other farinaceous foods, yet his book served a useful purpose by focussing attention on the rice question.

A thorough revision and extension of the existing state of knowledge of the cause of the disease was carried out by Fraser and Stanton in the Malay States (1911). They tested and examined every detail and really established the cause of the disease as the absence of some unknown substance in the food. They examined every sort of rice used in Malay, home-grown and imported, and the various methods of its preparation for food.

The whole rice grain or padi consists of four parts: the external husk; the pericarp, or thin covering skin of the seed; the germ or embryo plant; the endosperm or store of food for the young plant. The endosperm forms the greater part of the grain and consists chiefly of starch. The outer endosperm layers contain the so-called aleurone

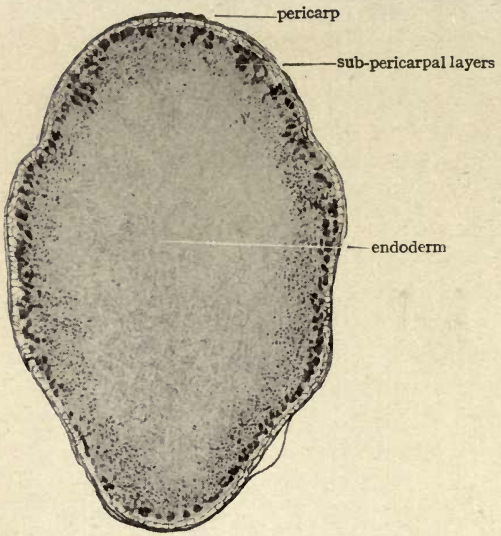

FIG. 1.—Transverse section of whole rice grain (husk removed) showing intact pericarp.

FIG. 2.—Transverse section of white (polished) rice grain. Pericarp and most of sub-pericarpal layers have been removed. It consists almost entirely of starch.

Reproduced by kind permission of Drs. Henry Fraser and A. T. Stanton from "Etiology of Beri-Beri," Study No. 12, Institute for Medical Research, Federated Malay States, 1911.

grains, composed of protein, fat, and other substances; this part of the grain is of special significance and is known as the subpericarpal layer. The germ lies at one end of the endosperm, from which it easily becomes detached if the pericarp be removed. The removal or retention of the pericarp, subpericarpal layer and germ is the main difference in the various processes of preparing the grain for food. The structure of the grain is shown in Figs. 1 and 2.

Rice as prepared by the Malays, and by the natives of the Philippine Islands, is pounded at home by hand until the husks are detached and can be blown away. Some of the pericarp is removed by this process, but if it is dark in colour the rest is often picked off by hand, as white rice is preferred. The hand-milling does not interfere with the germ and subpericarpal layer, the essential parts of the grain.

Polished (or uncured) white rice is prepared in machine mills and is the rice commonly sold in England. The rice bran, or polishings, contains the pericarp, germ and most of the outer layers of the endosperm; it is used as pig and cattle food.

Parboiled (or cured) rice is prepared by soaking in water for forty-eight hours and then steaming for five minutes (= curing). This process causes the pericarp and germ to adhere to the endosperm, so that they are not completely removed by the subsequent machine-milling. The final product is yellowish and translucent, and often has an unpleasant smell; it is therefore avoided by the Malays and Chinese settlers, who suffer in consequence from beri-beri; it is only used by the Indian settlers (Tamils), who are thereby protected from the disease.

These two kinds of rice were tested by Fraser and Stanton on 500 Javanese coolies employed on road construction in Malay and living in the virgin jungle far from any village or town. The men were examined carefully and all found to be free from beri-beri. After an interval

allowed for any latent cases to develop, so that the possibility of infection was excluded, they were separated into two groups, one party on the favourite white polished rice and one party on the distasteful parboiled rice. The daily ration also contained small quantities of dried salt-fish, onions, potatoes, coconut oil, tea and salt; the diet satisfied the standards for energy value and quantity of protein. There were no cases of beri-beri among 273 men on parboiled rice, but there were 20 well-marked and numerous slight cases among 220 men on white polished rice. No case of beri-beri occurred in anyone who had been less than 87 days on white rice. No evidence of any infective agent could be found; the beri-beri patients were in contact with the healthy men fed on parboiled rice and the disease was not communicated. Outbreaks of beri-beri amongst porters fed on white rice were stopped by substituting parboiled rice. All the evidence thus pointed to white rice as the sole causative agent.

No important chemical difference in the two kinds of rice could be detected, but Fraser and Stanton brought forward a most final and conclusive piece of evidence by showing that a small amount of an acid or alcohol extract of rice polishings added to a white rice diet prevented or cured birds suffering from the disease described by Eijkman. They thus proved that an unknown chemical substance is a necessary constituent of the diet; if it is absent, beri-beri develops.

The investigations of Vedder and his colleagues in the Philippine Islands, in which there was a large mortality from beri-beri, confirmed those of Fraser and Stanton. Vedder found that the poorer grades of white rice, which were not milled and polished with such care as the better grades, were equivalent to parboiled rice as a preventive of beri-beri. The native troops, or Philippine Scouts, who had suffered much from the disease, were completely freed from it in 1910 by the substitution of under-milled rice for white rice at the instigation of Major Chamberlain.

The main difficulty was to secure sufficiently under-milled rice, as the factories generally carried the milling process too far, and each fresh lot of rice had to be tested before issue. It is interesting to know that this is easily done by staining a sample with a solution of iodine; the highly milled grains stain almost black; grains still protected by some pericarp stain a light grey colour.

In spite of all the evidence that polished white rice was the cause of the disease, scepticism still existed. Strong and Crowell in 1912 therefore carried out another experiment. They were able to use 29 prisoners under sentence of death at Billibid prison. The prisoners were isolated and every precaution taken to exclude the possibility of infection. Beri-beri developed in 13 out of 17 prisoners fed on white rice, but there was only one doubtful case amongst prisoners fed on whole unmilled rice. Strong and Crowell were thus convinced that the disease was of dietetic origin.

Beri-beri is more prevalent at certain seasons. The seasonal epidemic appears at different times in different countries and bears a direct relation to the available food supply. Vedder found that in the Philippines the incidence of the disease was dependent upon the rice crop; if last season's supply of home-grown, hand-milled rice were used up before the new one was ready, imported highly-milled rice had to be used until the next harvest, and the cases of beri-beri were more numerous the longer this interval.

The Occurrence of Beri-beri on a Diet containing White Flour.

Beri-beri follows from a diet consisting largely of white wheaten flour. Several epidemics have been described by Little in Labrador and Newfoundland, where white bread is the chief food during the winter months; beri-beri appears in the spring. In the old days when brown flour was used there was no beri-beri in these countries.

A remarkable incident is related by Little. In 1910 a ship laden with a cargo of wholemeal wheat flour ran ashore on the coast of Newfoundland. In order to refloat the ship a considerable portion of flour was removed and used by the population in the neighbourhood. No case of beri-beri was reported in that district for more than a year after the wreck.

Beri-beri became a common disease in Norwegian ships after the use of white wheaten flour was made compulsory through the mistaken idea that it would help to ameliorate the men's hard life at sea. Previously they had eaten biscuits made from rye flour and had not suffered from beri-beri. The explanation is that in the milling of rye there is no separation of the germ which contains the antiberi-beri substance, but the germ is lost in the milling of white wheaten flour. Holst tells an amusing story of an old sea captain. In 1894 the masters of Norwegian sailing ships were compelled to supply their men with white wheaten flour; objecting to the new regulation, this old captain continued to use rye flour for his own food. Beri-beri appeared amongst his crew and the sick men were cured by rye biscuits from his private supply.

The occurrence of beri-beri amongst the British troops in the Dardanelles and Mesopotamia during the War is easily explained. The deficiency of the antiberi-beri substance in highly-milled wheaten flour is made good, under ordinary circumstances, by other articles in the diet, such as eggs, fruit and vegetables. The " mixed " diet, on active service far from a base, consists chiefly of non-perishable or sterilised foods, such as white flour, tinned meats, white rice, jam, sugar, cheese, margarine and salt fish. The deficiency in the white flour is thus not compensated for by the other articles in the diet, the antiberi-beri factor having been destroyed by heat during the preparation of the " tinned " ration of meat and vegetables (see table, p. 57). The Indian troops were protected from beri-beri by the use of *dahl* (= dried pulse) and by *atta* (= wholemeal flour). This is particu-

larly well illustrated in the report of Major-General Hehir on the health of the troops during the siege of Kut. The Indian troops never suffered from beri-beri, but there was beri-beri amongst the British troops during the early days of the siege; it disappeared later. Beri-beri followed upon the use of white flour, and when this was exhausted the British had to fall back on the coarse wholemeal wheat and barley flour used by the Indians, and the disease was cured. The reason for the disappearance of beri-beri was not appreciated at the time.

Ashmead, in 1901, mentioned the prevalence of beriberi amongst Scottish crews who were large consumers of oatmeal; in Brazil the disease follows upon the too exclusive use of manioc (tapioca).

Beri-beri cannot therefore be dismissed from consideration as a tropical disease peculiar to rice-eating peoples; large eaters of white bread and other prepared farinaceous foods also suffer from it if other protective food-stuffs are not taken.

Although a few medical men still cling to the belief that beri-beri is caused by an infection, or by a toxin, the majority agree that the disease is of dietary origin; this is shown by the resolutions passed by the section of Tropical Medicine at the International Medical Congress in London, in 1913:—

"(1) Beri-beri amongst natives living principally on rice is brought about by the continued and too exclusive use of rice, submitted to a too complete milling, which removes cortical and sub-cortical layers of the grain.

"(2) All authorities charged with the health of native communities are urged by every means in their power to restrain the use of this rice in the dietary of coolies.

"(3) In view of the proved non-infectiousness of beriberi, the section suggests that all port and sanitary authorities should abolish foreign quarantine and other restrictive measures against this disease."

Distribution of the Antiberi-beri Substance.

The work of the several investigators has shown that foods can be divided into two groups :—

Those containing Antiberi-beri Substance.	*Those not containing Anti-beri-beri Substance.*
Rice polishings (= rice bran).	Polished white rice.
Under-milled rice (= un-polished).	Sago.
Potato, whole.	Tapioca.
Beans, dried.	Peeled barley.
Barley, whole.	Sterilised foods.
Rye flour.	
Milk.	
Yeast.	

Infantile Beri-beri.

For many years beri-beri was considered to be a disease to which only adults were subject. Hirota (1888) was the first to describe in infants a condition closely resembling adult beri-beri, and his observations were confirmed later by other Japanese physicians. The disease known as *taon* or *suba* in the Philippines, which causes a very high infant mortality, has been found to be identical with infantile beri-beri described by Hirota in Japan. A special investigation, organised by the Philippine Bureau of Health (1909), showed that of all the infants under one year of age 56·6 per cent. died from this disease. Amongst the poorer classes many mothers lost five or six children from it. Nine-tenths of the deaths from this disease occurred between the ages of one and three months, and less frequently up to ten months of age.

It is a peculiarity of the Philippine Islands that 75 per cent. of the infant deaths are amongst the breast-fed, chiefly from infantile beri-beri; in Europe, and practically everywhere else, this proportion is reversed and the greater mortality is amongst the artificially fed infants.

This disease in infants was first attributed to some poison in the mother's milk, but later it was proved to be the result of a deficiency of the antiberi-beri substance in her milk, because her diet is poor in this substance. The natives believe that food is eaten merely to satisfy hunger and not to supply material for flesh and blood; if they have no sensation of hunger they think they are well-fed, and are therefore perfectly content with their filling diet of white rice. Women with well-developed beri-beri seldom become pregnant; some whose diet is just on the border-line of deficiency conceive and produce plump and apparently well-nourished babies. The diet, just sufficient to maintain the woman before pregnancy, is inadequate for the needs of both mother and child, and beri-beri may develop in the mother during pregnancy or lactation. Her nursling becomes restless and sleepless, its face is usually very full, and there is a blue look round the mouth and nose; the plump limbs pit on pressure (œdema). The child appears out-of-breath; the voice alters and may be lost. Finally the child dies from convulsions or heart-failure. The right side of the heart is much dilated and displaced to the right as in adult beri-beri.

The child's condition can be relieved only by a change of food. Artificial feeding is not practicable amongst these people because of their poverty and ignorance. Formerly the only chance of saving the child's life was to transfer it to a healthy wet nurse, but, since the recognition that the disease is caused by something lacking in the mother's milk, it has been possible to cure the child while still suckled by the mother, by giving the infant an extract of rice polishings. This fact proves once again that the disease is not caused by a poison in the milk.

Andrews quotes the case of a young woman and her infant both suffering from beri-beri, the mother so paralysed that she could not walk. In hospital the mother continued to suckle her baby, who received no other food, but the woman was given under-milled rice instead of

polished rice and also some *mongos*, a kind of bean similar to the cow-pea of the United States. Both mother and child made a rapid recovery, and after only twenty days were discharged cured.

The Philippine doctors now recognise the value of changing the mother's diet, but as under-milled rice cannot be bought in the open market, they advise the use of *mongos* in its place.

The Philippine Government passed a Bill in 1914 to provide money for the free distribution of extract of rice polishings to the suffering children. The extract, if given in time, produces a disappearance of all the symptoms as if by magic. At the end of three days' treatment the child is quite well except for loss of voice, which may not return for some months.

Polyneuritis in Birds and Animals.

The actual identity of polyneuritis in birds and of beri-beri in man cannot be indisputably proved, but there is much evidence to suggest that both diseases have a common cause, that is the absence of the same unknown chemical substance from the food. Absolutely identical symptoms cannot be expected in different species; even in cases in which the same cause is known to operate, as in the injection of a certain poison or of a particular type of bacterium, the symptoms produced in different species are not identical.

Experiments on birds with polyneuritis have certainly justified the application of similar methods for the prevention and treatment of beri-beri in man. Birds are apparently much more susceptible than man to a shortage of the antiberi-beri substance, and show signs of the disease on a diet which does not produce beri-beri in man; that this is a difference of degree rather than of kind is proved by the fact that foodstuffs which will prevent and cure polyneuritis in birds will also prevent and cure beri-beri in man.

The disease in birds resembles "dry" beri-beri;

FIG. 3.—Polyneuritis. First day of disease.

FIG. 4.—Polyneuritis; severe case. Second day of disease.

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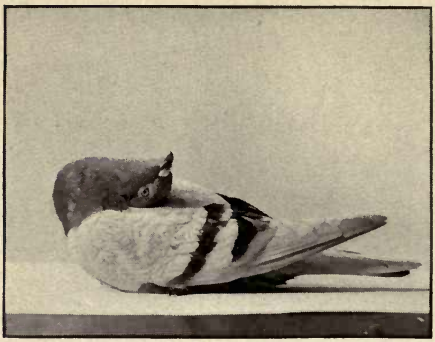

FIG. 5.—Pigeon suffering from polyneuritis.

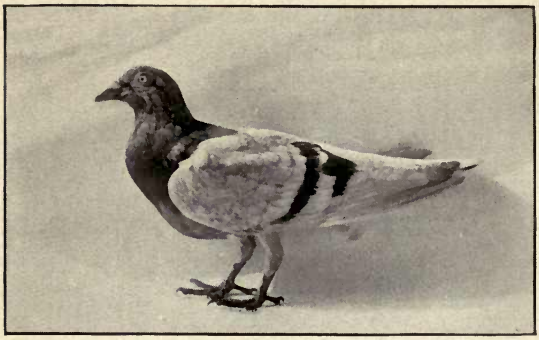

FIG. 6.—Same pigeon cured by treatment with B-Vitamin.
(From photographs kindly supplied by Dr. Drummond.)

paralysis is the most marked feature, and there is no œdema. At first the bird shows a peculiar high-stepping gait not observed in any other disease of fowls. The bird " teters " forward on its toes and stumbles if hurried; the voice is often lost. Paralysis of the legs increases rapidly till at length the bird can only lie on its side—in farmyard phraseology " off its legs " (Figs. 3 and 4). Wing-drop is seen in some birds in the early stages, and later the head may be drawn back and the whole body convulsed. Paralysis of the swallowing muscles may cause death from starvation.

The disease develops at different rates, depending partly on individual susceptibility, but chiefly on the degree of deficiency of the diet. Definite symptoms do not appear on unpolished rice alone before twenty to thirty days. On a diet affording considerable protection, Eijkman recorded a case which took more than a year to develop.

Recovery is extraordinarily rapid if the bird is treated with some special food, such as extract of rice polishings, when it is first off its legs; chronic cases of long standing are generally impossible to cure (Figs. 5 and 6).

The hypersensitiveness of birds to a shortage in their food of the protective substance against beri-beri, needs to be better appreciated by poultry-keepers. Delicacy in young chicks, as shown by so-called leg-weakness, or by increased susceptibility to infection, may be traced in some cases to a diet deficient in the antiberi-beri substance, such as cereals free from germ which are frequently used for birds.

A characteristic neuritis has been produced experimentally in dogs, goats, pigs and monkeys; the latter also showed the œdema and heart symptoms of beri-beri. An experiment was devised by McLaughlin and Andrews in which puppies were suckled by Philippine women whose infants had just died of beri-beri. The puppies developed unmistakable signs of the disease.

Beri-beri has been observed in animals on board ship in which the crew had beri-beri.

CHAPTER III

SCURVY (OR SCORBUTUS) AND THE ABSENCE OF FRESH FRUIT AND VEGETABLES

ALMOST every generation of mankind has suffered from the terrible disease of scurvy. Its cause can be definitely traced to the absence of fresh food, particularly of juicy fruits and vegetables. As long ago as 1734, Bachstrom wrote :

" From want of proper attention to the history of scurvy its causes have been generally, though wrongfully, supposed to be cold in northern climates, sea air, the use of salt meats, etc., whereas this evil is solely owing to a total abstinence from fresh vegetable food and greens, which is alone the true primary cause of the disease. And where persons, either through neglect or necessity, do refrain for a considerable period from eating the fresh fruits of the earth and greens, no age, no climate, or soil are exempt from the attack. Recent (*i. e.* fresh) vegetables are found alone effectual to preserve the body from this malady; and most speedily to cure it even in a few days, when the case is not rendered desperate by being dropsical or consumptive." [1]

Symptoms.

There is a remarkable uniformity in the symptoms of scurvy. The onset is foreshadowed by a feeling of great fatigue, not dissipated by sleep; there is headache and a general disinclination for exertion of any sort; the complexion changes to a pallid dusky hue. At an early stage transient pains in the joints and limbs are felt, and in the absence of any other symptoms, are often wrongly regarded as rheumatism; but in scurvy the pain and swelling are the effect of hæmorrhages into the tissues which may occur in any part of the body. Small hæmorrhagic spots (petechiæ) appear round the hair follicles of the legs, and patches like bruises of varying size appear on the skin, particularly where

[1] Lind's translation.

there is any kind of pressure. Larger hæmorrhages occur in the most frequently used muscles. Intense pain is caused by hæmorrhages between the limb bones and their covering membranes, so that the limbs cannot be moved on account of the pain. There is often bleeding from the nose. In well-defined cases the gums are almost invariably affected; soft spongy swellings sprout up between the teeth and are followed by ulceration and hæmorrhages of the gums. The teeth become loose and may fall out; the breath is very fœtid. Unless the progress of the disease is arrested by a timely change of diet it ends fatally.

The disease usually makes its appearance after four to six months on a scorbutic diet. The most fearful effects of scurvy have been evident at times of famine, during sieges and among sailors on long voyages. It has been an accompaniment of every war from the time of the Crusades up to the last great war; yet history books are strangely reticent as to the ravages of scurvy, which had such a determining effect upon the result of campaigns that scurvy was a political factor of no mean importance. In our school-days we did not realise that Vasco da Gama only achieved his pioneer voyage round the Cape of Good Hope to the East Indies at the cost of 100 deaths from scurvy out of a crew of 160 men. Neither did we realise that France at the beginning of the seventeenth century had seriously to consider relinquishing her colonies in North America, so numerous were the victims of scurvy there. Writing in 1755, Dr. James Lind said, " Armies have been supposed to lose more of their men by sickness than by the sword, but this observation has been more than verified in our fleets and squadrons, where the scurvy alone during the last war proved a more destructive enemy and cut off more valuable lives than the united efforts of the French and Spanish arms." These are but a few instances of the destruction caused by scurvy.

The disease is still endemic among the civilian population of Northern Russia, and in the dry parts of the Australian bush a disease called " Barcoo rot " is probably a mild form of scurvy. Epidemics have always been

most frequent after long winters; scurvy has never existed in southern latitudes where fruit and vegetables were used abundantly all the year round. In England during the Middle Ages the food of the people in the winter was nearly as devoid of fresh meat and vegetables as the food of sailors on long voyages. Swede turnips and other roots for feeding live-stock during the winter were not grown, and the animals, except those required for breeding purposes, were slaughtered in the autumn and their flesh preserved with salt and spices. Salt meat had to be used for about nine months in the year, and the customs of game-preserving and pigeon-breeding by the large landowners originated, not to provide sport, but to furnish the lords of the manor with fresh flesh during the winter as a relief from the perpetual salt food. Green vegetables seem to have been little relished, and when Henry the Eighth's wife, Catherine of Aragon, desired a salad, a gardener had to be imported from Holland to grow it for her. Potatoes, introduced during the Elizabethan era, were at first only used as food for pigs or by the very poorest classes. In the early seventeenth century Harvey referred to scurvy as "the disease of London"; it would thus appear to have been more prevalent there than in the country. As gardening and agriculture improved, scurvy became less and less frequent, until finally it was almost entirely confined to ships, armies on active service, prisons, asylums and after famines.

The *Treatise on the Scurvy* published by Dr. James Lind in 1755 contained all the historical and medical information which he could collect on the subject, together with his own extensive experiences and experiments on long voyages as ship's surgeon. The book was a valuable contribution to scientific literature. Lind freed himself from the inherited dogmas which then fettered the progress of medical knowledge; he examined all evidence with an open mind, rejecting theories which could not be substantiated by facts. His final conclusions as to

the cause and cure of scurvy are essentially sound and in accordance with the earlier observations of Bachstrom. The medical men of that period were not encouraged to observe facts and reason scientifically, but were either weighed down by the accumulated tradition of many years, or given over to fanciful imaginings which led them to classify scurvy into hot and cold scurvies, acid and alkaline scurvies, and land and sea scurvies, and to suggest many weird and wonderful methods of treatment. Certain passages in Lind's book suggest that traditional beliefs were as difficult to combat then as they are now: "Some persons cannot be brought to believe that a disease so fatal and dreadful can be prevented or cured by such easy means. They would have more faith in some elaborate composition, dignified with the pompous title of an antiscorbutic golden elixir or the like. Facts are sufficient to convince the unprejudiced. It is no easy matter to root out old prejudices or to overturn opinions which have acquired an establishment by time, custom and great authorities."

Lind does not seem to have received any public honour for his valuable work, but a few years later Captain Cook was awarded the Copley Medal of the Royal Society because he had maintained good health and freedom from scurvy amongst his seamen on long voyages. It is probable that Captain Cook would not have accomplished his voyages so successfully without Lind's work. The latter was a pioneer in experimental investigation; his experiments were carried out on men and not on the lower animals. In 1747, on the ship *Salisbury*, he took out to sea twelve patients suffering from the scurvy with symptoms as similar as he could have them.

"They were all kept together in one place and fed upon the same diet of water gruel sweetened with sugar, mutton broth, light puddings, boiled biscuit and sugar, barley, raisins, rice, currants, sago, wine, or the like. In addition two had a quart of cyder daily; two had 25 drops of elixir vitriol three times daily upon an empty stomach; two had 2 teaspoonfuls

of vinegar three times daily upon an empty stomach; two had a course of sea water, half a pint every day; two had each 2 oranges and 1 lemon which they ate with greediness; they continued for six days on this course, having consumed the quantity which could be spared; two took the bigness of a nutmeg three times a day of an electuary recommended by an hospital surgeon, made of garlic, mustard seed, red raphan, balsam of Peru and gum myrrh; using for common drink barley-water well-acidulated with tamarinds, by a decoction of which, with the addition of cremor tartar, they were gently purged.

"The consequence was that the most sudden and visible good effects were perceived from the use of oranges and lemons; one of those who had taken them being at the end of six days fit for duty. The other was the best recovered of any in his position and was appointed nurse to the rest of the sick.

"Next to oranges the cyder had the best effect; the other remedies produced no improvement."

As a practical method of preventing scurvy on board ship Lind recommended the growing of cresses on layers of wet cotton.

Many subsequent epidemics of scurvy might have been avoided if the teachings of Lind had been put into practice. He laid much stress on the uselessness of dried vegetables as an antiscorbutic, yet after his time dried vegetables were repeatedly tried in the British Navy and found a failure; their use did not prevent scurvy in the American Civil War. The British public were exhorted during the last war to dry and preserve vegetables to send to our fleets and to our prisoners-of-war in Germany, that they might have so-called *fresh* vegetables; the intention was excellent but the ignorance lamentable.

Budd, in his series of lectures on *Disorders resulting from Defective Nutriment*, delivered in 1842, pointed out the failure to profit by past experiences as exemplified in the history of scurvy at sea :—

"On April 2nd, 1600, four ships left this country on an expedition for the establishment of the East India Company.

Scurvy prevailed to such a degree that in three of the ships one-quarter of the men died before reaching the Cape, and the rest were so weakened that the merchants on board were obliged to do the work of common sailors. A remarkable circumstance was noticed, which if laid hold of and turned to profit would have prevented many subsequent disasters. While three of the ships were so weakened by scurvy, the Commodore's own ship was in perfect health. This was attributed to his having given three tablespoonfuls of lemon-juice every morning to each of his men.

" The discovery of the virtue of lemon-juice as a preventive of scurvy was soon forgotten, or at least only remembered when chance again offered some striking proof of the efficacy of oranges and lemons. No practical advantage followed, the disease continued to devastate our Fleets until in 1795 an Admiralty order was given that every ship in His Majesty's Navy should have a supply of lemon-juice. The effect of this order was remarkable, the mortality fell suddenly and to a degree that can scarcely be credited by one who has not read the heartrending accounts of the sufferings occasioned by scurvy in the voyages of Lord Anson and our earlier navigators. Between the years 1771 and 1803 the sickness in the British Navy was reduced to almost one-quarter of its former proportion. Experience has established the efficacy of lemon-juice in curing and preventing scurvy. It is so cheap that it may well excite surprise that up to the present time (1842) no regulation has been made for compelling our merchant ships to take a supply of it. Every year a number of miserable beings are brought into our ports as if to show us the fidelity of the descriptions which the older navigators have left of their sufferings."

It indeed seems likely that the disease would have continued uninterruptedly to take its toll from the men of the merchant service, had not sailing vessels been gradually superseded by steamers, and the mortality from scurvy reduced by quicker voyages. The prevalence of scurvy in our prisons was attributed by Budd to the mistaken notions of its cause still entertained in spite of the earlier writings of Lind, Bachstrom and others.

The history of scurvy in the Polar regions affords other instances of the need for fresh food, but in these cases prevention could be secured by the consumption of *large*

amounts of fresh meat, often eaten raw. The following tale is told in the words of Dr. F. Millman (1772) :—

"In 1663 the Dutch Greenland Company left seven stout sailors to pass the winter in that country in order to get observations on the climate. They were plentifully furnished with provisions of every sort from the ships, but this provident care proved a very baneful store to them. Such an indigestible diet concurrently with the cold of so northern a latitude rendered them scorbutic, and they became miserable victims of the curiosity of their countrymen. Not deterred, however, by the fate of these unhappy men, the Dutch Company the year following repeated the experiment with the same event. It seemed extraordinary that they should have profited so little by the example of eight Englishmen, who were accidentally left there in 1630. Though wholly unprovided with any means of subsistence from June till the May following, but such as they could procure by their own address and industry, they not only kept free from scurvy but every one of them survived the disaster. They had neither bread nor biscuit. They had no sort of vegetable matter nor spirituous liquor. Their drink was water, their food chiefly the flesh of reindeer, of bears and other such wild animals as they could kill."

Stefansson's observations during the Canadian Arctic expedition in the winter 1916–17 has corroborated the accuracy of the experiences related above. The men were expected to live entirely on musk-ox, reindeer, seal and bear meat. Unfortunately a store, left from a 1910 expedition, of several tons of food consisting of flour, salt pork, butter, honey, sugar, pilot bread, glasses of preserved fruit, rice, beans and peas, was discovered. Those men who lived largely on reindeer and other meat, often eaten raw, did not get scurvy, but those who ate mainly of the provisions from the store got scurvy.

Nansen's expedition escaped scurvy by eating large quantities of fresh bear's meat, but Scott's Antarctic expedition, well-equipped with provisions from home, suffered severely from the disease. In the Jackson Harmsworth expedition to Franz Josef Land (1894–7) all the crew left on the ship, with tinned and salted meat as food and with lime-juice, got scurvy; the land

party lived for three years on fresh bear's meat without any scurvy.

Infantile Scurvy.

In the seventeenth century Glisson differentiated between rickets and scurvy in infants, but for more than two hundred years afterwards no further mention of infantile scurvy was made. Dr. (now Sir Thomas) Barlow in 1883 described peculiar symptoms in infants, distinct from rickets and allied to adult scurvy; previously these cases had been known as acute or hæmorrhagic rickets, but are now called Barlow's disease or infantile scurvy. Improperly fed children may suffer from both rickets and scurvy at the same time; such cases are still sometimes referred to as scurvy-rickets and wrongly believed to be a form of rickets. According to data collected by the American Pediatric Society, 45 per cent. of the cases of infantile scurvy are complicated by rickets; the dual symptoms are caused by a diet lacking in more than one respect. Scurvy is most common in infants fed on overheated or over-diluted cow's milk, alkaline food mixtures and certain proprietary foods. The disease is seldom seen in infants under four months of age; most cases occur during the ninth and tenth months; there is then a gradual decrease in the number of cases, and scurvy is rare in children after eighteen months.

Symptoms.

Many of the symptoms in infants resemble those of scurvy in adults. The child is frequently well covered with subcutaneous fat and does not appear ill-nourished. The first signs of ill-health may be digestive troubles, and almost invariably there is a marked pallor, intensified by blue rings round the eyes. Suddenly the child becomes fretful in a special kind of way; it is quiet as long as it is left alone, but cries continuously when bathed or moved. The pain is located in the lower limbs, and any attempt to move the leg or thigh causes a scream. Swellings of the lower limbs, first in one leg then in the other, may be detected. According to Holt four-fifths of the cases of infantile scurvy have at

first been mistaken for rheumatism on account of the swollen and tender limbs. The legs are not flexed as in the healthy infant, but limp and straight (see Fig. 7), and owing to their tenderness are kept so still that they seem to be paralysed. The bones are brittle from imperfect bone formation and do not bend as in rickets; the heads of the long bones may completely separate from the shafts. Characteristic changes take place in the microscopic structure of the tissue at the junctions between the rib-bones and cartilages. Hess has described cases of infantile scurvy not complicated with rickets, showing a beading of the rib junctions indistinguishable to the touch from the beading regarded as a specific sign of rickets (see p. 73). The nature of the beading, in the absence of other definite signs, can only be determined by the response to treatment: if the beading is due to rickets it disappears on treatment with cod-liver oil, if due to scurvy it is not cured by cod-liver oil but by orange-juice.

The gums of scorbutic infants with no teeth are pale and swollen or marked with purple patches; if there are several teeth the gums may be bleeding and spongy; if the gums are much affected the breath is very fœtid, as in adult scurvy. Nose-bleeding is a common sign; large bruises or small purple spots appear on the skin wherever there is any kind of pressure.

The swollen and tender limbs are due to hæmorrhages, either under the skin, in the muscles or between the bone and its sheath. Hæmorrhages may occur into the tissues of any part of the body; sometimes hæmorrhage behind the eyeball causes one or both eyes to protrude with almost startling suddenness. Blood may be passed with the fæces or urine; the latter is usually scanty in amount. Extensive hæmorrhages may produce a rise in temperature to 101 or 102° F., or even higher.

Barlow and others have recorded identical symptoms amongst children of two to ten years who had a curious hysterical dislike of vegetables and meat. Barlow treated scorbutic infants with undiluted fresh cow's milk, sometimes thickened with sieved potato, and a tablespoonful daily of orange- or grape-juice.[1] Chick and Dalyell, working among the famine-stricken children in Vienna,

[1] Recent work (see table, p. 61) has proved grape-juice to have only very slight antiscorbutic power; larger quantities than are practicable in infant feeding would have to be given. Orange-juice is cheaper and much more effectual.

have used swede-turnip-juice and tomato-juice with good results. Swede-juice is not popular amongst those in charge of the infants, as it sometimes produces looseness of the bowels.

Before 1892 few cases of infantile scurvy had been recognised in the United States, but now the disease is not considered rare, the increase being partly due to more accurate diagnosis, and partly to an actual increase following upon the extended use of proprietary foods and the more general commercial pasteurisation of milk. On both sides of the Atlantic, infantile scurvy is more common amongst the richer classes; the giving-'im-a-bit-of-what-we-'as-ourselves policy of the poorer people tends to prevent scurvy, though it may have other drawbacks. Dr. Northrup, at a time when infantile scurvy was still rare in the States, wrote a vivid description of the circumstances under which the disease commonly appears :—

"The patient was the offspring of wedded representatives of rich and powerful families in the fashionable and political worlds. There was no lack of love and devotion. The lack was in wisdom and judgment; the abundance—the nurse's self-esteem and ignorance; these allowed the present case and history to continue on to full accomplishment.

"The child was sixteen months, a girl. Thriving very well in early months; breast-fed four months. After this the child was fed on a proprietary food diluted with water and milk; by mistake too little milk was used. The child apparently thrived well, though backward in walking and talking. The teeth were normal; there was no sign of rickets. Three weeks previously (to consulting Dr. Northrup) the nurse had noticed some slight change in the child's gums. The family doctor ordered more milk to rectify the mistake, beef broth and iron peptonate. One week later there was trouble in the lower right limb, evinced by worrying sensitiveness on handling and a tendency to keep the limb straight. Rheumatism was diagnosed, but antirheumatic treatment had no effect. The parents went away for a fortnight and the doctor was not called in. The nurse drew no conclusions from the rapidly changing gums. The parents returned and found the child ill. (Dr. Northrup was now called in.) The child cried on seeing a strange face and became alarmed for the safety of its lame leg.

In the wry face of crying the little patient fairly unbuttoned from between its lips two rows of irregularly nodulated purple gums, from the summits of which the points of the teeth protruded. The gums were dark and bled freely in the act of crying from the compression of the lips alone. There was no nose-bleeding, nor purple spots on the skin, no blood in the urine nor from the bowel. Spongy gums and swollen thigh were the only symptoms. Confirmation of the diagnosis of scurvy was given by the success in treatment. The child was sent to the country and received fresh cow's milk, instead of the proprietary food, beef-juice and baked potatoes. The one thing which the child seemed to crave, for which it reached out, and which it seized with ravenous avidity, was the orange. The child could scarcely be restrained till it held the fruit in its grasp, and then proceeded to souse its lips and nose in the juice. Improvement began at once. The gums were normal in ten days, in a month the child could stand. Soon she appeared as a child small for her age, but as if nothing had ever been the matter with her."

In comparatively few cases do all the symptoms of infantile scurvy develop. One or more definite signs may be present and the correctness of the diagnosis confirmed by the response to treatment. If orange-juice is given, slight cases improve immediately and severe cases by the end of four days.

The acute form of infantile scurvy once seen is never forgotten, but it is not the common form of the disease. The usual form, described as subacute, latent, or incipient scurvy, shows a general falling off in health with no very definite symptoms. The infant, hitherto thriving, begins to ail, weight may be lost, the appetite is poor and the digestion disordered. The child becomes pale, fretful, sleepless and miserable, and sometimes feverish. The rapid improvement following two or three days' anti-scorbutic treatment shows that these symptoms are an indication of early scurvy. Slight tenderness of the thighs and a rim of crimson on the upper gums, perhaps behind an upper incisor, are often noticeable; the respiration and pulse are slightly quickened. This condition of latent scurvy is quite common in large cities, especially if the milk supply is pasteurised commercially and reheated

in the homes. In these cases the food contains sufficient antiscorbutic to prevent acute scurvy, but insufficient to ensure perfect health.

Experimental Scurvy.

Holst and Fröhlich were the first of the modern scientific investigators on scurvy; they wished to determine the cause of scurvy and beri-beri upon Norwegian ships. The work of Eijkman on beri-beri was well known to them, and their first work was practically a repetition of his experiments upon birds, but later they tried feeding experiments with other animals. They found that guinea-pigs fed on a diet of groats, grain, or bread died in about twenty-one days after having lost from 30 to 60 per cent. of their weight, with symptoms quite distinct from those of beri-beri or starvation, but resembling those of human scurvy, more especially infantile scurvy. No fresh vegetables or fruit had been given to the guinea-pigs, and it was found that the suffering animals could be cured by adding to their food any well-proved antiscorbutic, such as fresh cabbage, dandelion leaves, lettuce, endive, or cloudberries. As human beings do not eat raw cabbage, the effect of cooked cabbage was next tested on guinea-pigs. They all developed scurvy, but the symptoms were less severe than on the grain diet alone. Guinea-pigs thus appear to be more susceptible to scurvy than man, as it is by cooked vegetables that man is normally maintained free from scurvy for long periods of the year. The uselessness of dried vegetables as an antiscorbutic was confirmed by tests on guinea-pigs. Cloudberries, or raspberry-juice preserved by heating for a short time with sugar, were found to retain their anti-scorbutic property. Other experiments showed that dried peas, lentils and other pulses, so efficacious in preventing and curing beri-beri, were of no use in preventing scurvy. Some substance in growing vegetables thus appeared to be the active agent against scurvy. Holst and Fröhlich proved this by feeding guinea-pigs upon soaked and

germinated peas, lentils, barley and other grains; they were protected from scurvy.

There seemed only one explanation to all these results, an explanation put forward by Budd in 1840, that " the cause of the disease is due to some essential element which he hoped the chemist would soon isolate." Holst and Fröhlich practically proved Budd's theory to be correct. Further work is described on pp. 58–61 and pp. 66–69.

Scurvy during the War.

At the beginning of the War there was sufficient evidence available of the cause and cure of scurvy, and also of beri-beri, to have prevented these diseases from incapacitating many men. In spite of this there were outbreaks of scurvy amongst our troops in camp at home, in France and in the East which might have been avoided. On the whole there was little scurvy amongst the British troops in Europe. The Mesopotamia Commission Report records that 7500 men were lost to the force in nineteen weeks in 1916 from scurvy; it was almost entirely confined to the Indian troops, which had altogether 14,000 cases from 1916 to 1918. Vegetables, meat and milk, the ordinary antiscorbutics in the Indian diet, were generally not obtainable on field service and in their absence signs of scurvy appeared in four months at latest. The disease was speedily curable at an early stage, but increasingly difficult after delay. In Amara, where unlimited quantities of milk curds were available, incipient scurvy disappeared. The scorbutic condition prevented the healing of wounds and favoured the formation of pus, a fact which had been recognised by our Navy surgeons in the old days. In 1803 Sir Gilbert Blane wrote: " It is found from direful and multiplied experience that not only those who are affected with actual symptoms of scurvy, but those who are exposed to the causes of it, are peculiarly susceptible to ulcers of the most malignant kind from the smallest injury which breaks the skin. The peculiar susceptibility

of sailors to this complaint is no doubt owing chiefly to their diet."

During the siege of Kut the British troops suffered from beri-beri, while the Indians were protected by their coarse wholemeal flour (p. 22), but there were 1050 cases of scurvy amongst the Indians and only one amongst the British. The protection of the British troops from scurvy was attributed to their ration of horse-flesh, which was refused by most of the Indians. As soon as wild herbs, shrubs and grass sprang up at the end of February in sufficient quantities to be cooked and eaten, the incidence of scurvy declined in spite of semi-starvation.

Scurvy in Mesopotamia became rare towards the end of the campaign, as the Arabs were encouraged to make gardens and sell vegetables; Government gardens were also established in which radish, leeks and spinach were grown. The Indians were advised to germinate their dahl (that is, lentils and other pulses), which formed a large part of their food.

In some parts of Russia and Central Europe, both during and after the War, scurvy was widespread among troops and civilians owing to the impossibility of getting a proper food supply. Russia was the country most afflicted, but after that came Roumania, where scurvy was very prevalent among the German, Austrian and Turkish troops. Epidemics of scurvy were also reported from Bulgaria, Serbia and Turkestan. An epidemic with many deaths among the civilians in Petrograd in 1916 was attributed to the extensive use of frozen meat and spoiled potatoes.

In the extreme north of Russia scurvy is always endemic during the winter; many cases were observed by the medical officers with the British Expedition on the Murmansk coast amongst the Russian peasants. The Laplanders in the same district escaped scurvy, as they used much more fresh meat and less cereals and preserved food than the Russians. Amongst the British Force in the Murmansk region there was little scurvy; many

cases of debility and depression were believed to be mild scurvy, but a severe epidemic was warded off by the use of germinated peas and beans as recommended by Chick and Hume (p. 59).

Capt. A. J. Stevenson, R.A.M.C., carried out an experiment on the scorbutic inmates of a Russian civilian prison to test the curative value of different food-stuffs. The prisoners were divided into six groups of six patients, each group receiving the same scurvy-producing diet, but a different curative food-stuff. The following were given daily to—

Group (1) 4 oz. fresh lemon-juice.
(2) 8 oz. germinated peas, cooked half an hour.
(3) 8 oz. germinated beans, ,, ,, ,,
(4) 10 oz. fresh underdone meat.
(5) 8 oz. tinned fruits.
(6) 2 pints of lactic acid milk prepared by inoculating with lactic acid bacteria and leaving for thirty-six hours till nearly solid.

All groups showed marked improvement, but it was most rapid with the lemon-juice, sour milk and germinated peas. The peas were palatable, but the beans were disliked and caused indigestion.

There was much scurvy amongst the Serbian troops; Wiltshire reported 3000 cases. The available peas and lentils were not suitable for germination as they had been decorticated. A supply of beans was at length received; they were soaked in water for twenty-four hours, placed on trays and kept damp, but exposed to air till they began to sprout. The germinated beans were boiled for ten minutes. Their antiscorbutic value was compared with that of lemon-juice: 30 scurvy patients were given 4 oz. each of fresh lemon-juice daily; 27 others in slightly worse condition were each given 4 oz. (dry weight) of germinated beans daily. The beans looked and smelt unappetising, and considerable prejudice had to be

overcome, as the Serbs regarded beans as " pigs' food." The condition of the gums was taken as the index of recovery. In those on beans the gums returned to normal in an average of 3·1 weeks as against 3·4 in the lemon-juice patients. Scurvy was reported at times amongst the French and German troops on the West Front. In 1917, Harvier, a French medical officer, discovered that 95 per cent. of the 800 men in his charge were suffering from scurvy. The cases of scurvy amongst German prisoners captured on the West Front at the beginning of 1917 were at first wrongly diagnosed as " purpuric rheumatism." On the East Front, especially among the Russian troops, scurvy rendered many men unfit for service and generally lowered the resistance to infection and delayed the healing of wounds.

Some of the records of outbreaks of scurvy in Europe describe œdema and neuritic pains in the legs; these are symptoms of beri-beri and not of scurvy. It is therefore probable that a certain amount of unrecognised beri-beri was present associated with the generally disorganised food supply. Fuller reports may definitely show that both these diseases occurred amongst troops and civilians to an extent quite unappreciated at the time. The various defects in the quality and quantity of the food would account for a commingling of symptoms which would obscure the clear-cut picture of either beri-beri or scurvy alone. At various times much has been written about " the affinities " of beri-beri and scurvy, but they are distinct diseases due to different deficiencies in the diet, and if they occur at the same time in the same patient, they can always be traced to a diet lacking in both the antiberi-beri and antiscorbutic vitamins.

CHAPTER IV

THE DISCOVERY OF THE ACCESSORY FOOD FACTORS, OR VITAMINS

THE accessory food factors were discovered by physiologists and biochemists who were investigating the function in nutrition of the individual groups of food substances such as "pure" protein, fat, salts, etc. The pure substances were prepared in the laboratory and their effect upon the body tested by feeding experiments. A convenient protein for this purpose is the casein of milk, for not only can it be easily prepared, but also several preparations consisting almost entirely of this protein can be purchased. These commercial preparations are salt-free, and, after extraction with alcohol and ether to remove fats and lipoids, consist of practically pure protein. Pure proteins can also be prepared from egg white, blood serum, nuts, legumes, cereals, etc. Many "pure" carbohydrates are available: starch, dextrin, cane sugar, milk sugar, grape sugar. Lard is generally regarded as the purest fat; other pure fats are olive oil and cotton-seed oil. A mixture of salts has generally been compounded from the purest chemical specimens, this mixture being made to resemble in quantity and proportion the mineral constituents of a normal diet. Sometimes the ash of the animal's normal diet is used instead of a salt mixture.

One of the earliest feeding experiments on animals was made by Lunin (1881) to study the effect of salts in the food. He fed mice upon a diet of specially prepared milk fat, casein and cane sugar; some mice were given salts in addition and others had no salts. Both sets of mice died within thirty-six days, but other mice, used as a control,

fed on fresh milk alone, lived and grew normally. Lunin concluded from these facts that " other substances indispensable for nutrition must be present in milk besides casein, lactose, fats and salts."

Many independent workers have since confirmed Lunin's results and found it impossible to keep animals for any length of time on artificial diets intended to contain everything essential to life. The failure was attributed to confined space, absence of fresh air and the monotony of the diet, but these suppositions did not explain the fact that animals lived in good health under exactly similar conditions of confinement on a monotonous diet of a natural raw product such as milk or egg.

The discovery of some substance, or substances, in the food other than protein, carbohydrate and fat, which were essential for the life of animals, was made by Prof. F. G. Hopkins; the work was published in 1912, but had been carried out some years earlier and delayed by his ill health. Hopkins kept two sets of young rats, approximately 1 to 2 ounces in weight, on a basal diet consisting of purified casein, lard, sugar and salts derived from the ash of oats and dog biscuits, the animals' previous food. The experimental diet satisfied physiological requirements in respect to protein, fat, carbohydrate, salts and energy value. One set of rats was given in addition 2 to 4 c.c. of milk daily, fed by hand, so that it was definitely known to be consumed. The other set had no milk. The set with milk grew normally; the non-milk set declined in weight after ten to fifteen days.

The same experiment was repeated in an even more striking fashion. Eight rats were used in each set; eighteen days after those without milk had begun to decline in weight they were given milk, and the other set had their milk discontinued. The original milk set now declined in weight, but growth began again in the other set. The results were most graphically illustrated by their weight charts (Figs. 8 and 9).

In discussing these results Hopkins wrote :

"It is possible that what is absent from artificial diets and supplied by such addenda as milk and tissue extracts is of the nature of an organic complex (or complexes) which the animal body cannot synthesise. But the amount which seems sufficient to secure growth is so small that a catalytic or stimulative function seems likely. . . . Stimulation of the internal secretions of the thyroid and pituitary glands, which

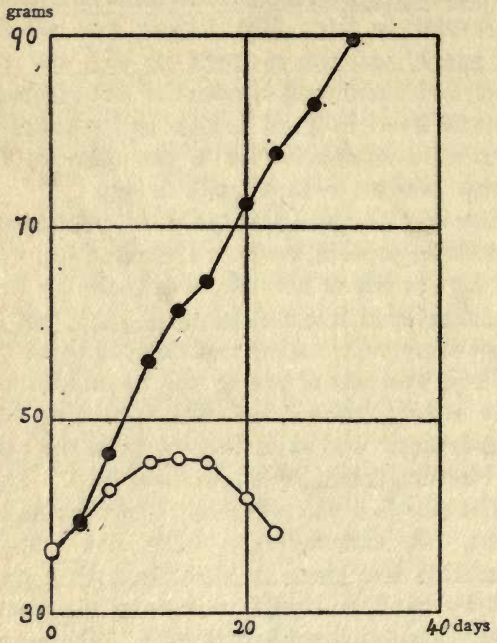

FIG. 8.—Lower curve is the average weight of six rats on artificial diet alone. Upper curve, six similar animals receiving in addition 2 c.c. milk per day.

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are believed by very suggestive evidence to play an important part in growth processes, can be legitimately thought of. On the other hand the influence upon growing tissues may be direct. If the attachment of such indispensable functions to specific accessory constituents of diets is foreign to current views upon nutrition, so also is the experimental fact that young animals may fail to grow when they are daily absorbing a sufficient quantity of formative material and energy for the purpose of growth."

Hopkins termed the unknown substances *accessory food factors*.

At the time that Hopkins was carrying out these experiments upon rats, Stepp in Germany tried to find out if animals could live without fat or lipoids in their food. He found that mice could live for months on a diet of bread

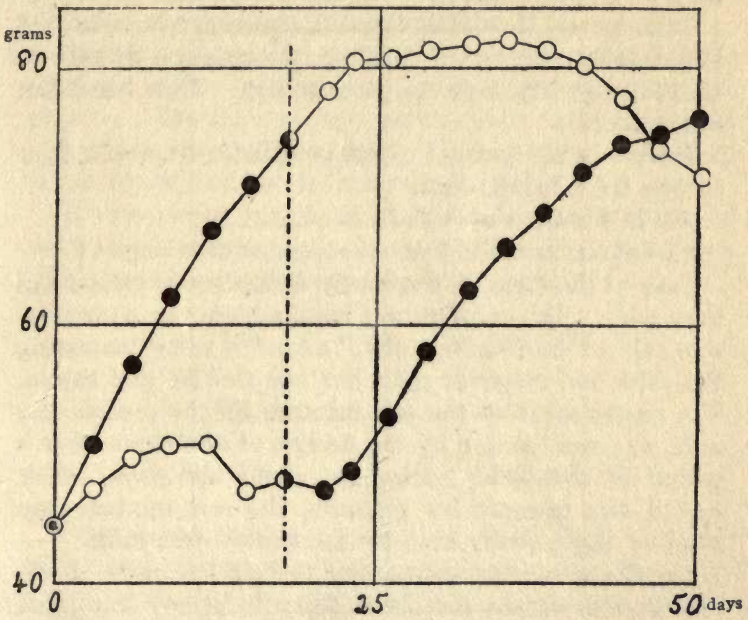

FIG. 9.—Lower curve (up to 18th day) shows average weight of 8 rats upon pure dietary; upper curve 8 similar rats taking 3 c.c. milk each day. On the 18th day, marked by vertical dotted line, the milk was transferred from one set to the other.

[1] Reproduced by kind permission from the *Journal of Physiology*, 1912, **44**, 433.

made with milk, but that they only lived for a few weeks if the same food were first extracted with alcohol and ether to remove the fat and lipoids. On adding the extract to the extracted food, the diet again sufficed for normal nutrition. Stepp at first thought that the substance essential for growth removed in the extract must be a lipoid, but on adding in turn all the known lipoids to a

diet of extracted food he failed to maintain the mice. By continued experiments he proved that the missing substance was neither fat, lipoid, nor salt, nor any known chemical substance, and he concluded that " the unknown substance indispensable for life may go into solution with the lipoids, and that the latter thereby become what may be termed ' carriers ' for this substance."

Osborne and Mendel in America, since 1911, have carried out a large number of feeding experiments on rats to study the quality of protein in nutrition. Their basal diet consisted of—

Protein in the form of casein (or gliadin from wheat, or edestin from hemp, etc.).

Fat in the form of lard.

Carbohydrate in the form of starch or cane sugar.

Salts in the form of a carefully compounded mixture of pure salts. This mixture was replaced later by a preparation called " protein-free milk," a kind of whey containing the salts and sugar of milk but not the fat and casein. The replacement of the salt mixture by the protein-free milk was necessitated by the decline of adult rats after a period of well-being lasting for about 290 days; their health was restored by replacing the salt mixture and some of the carbohydrate by the protein-free milk.

On the same diet containing protein-free milk young rats grew normally for about forty to eighty days, but then a decline set in and the animals died unless put back on normal food. The decline could also be arrested by the substitution of whole-milk powder for pure protein. Like Hopkins and Stepp, Osborne and Mendel were forced to conclude that whole milk supplied some special substance essential for life. Further investigations showed that this growth-promoting substance was contained in the fat of milk, but not in the other milk solids nor in the water of milk. Other fats were then tried; egg fat or cod-liver oil were as good as butter fat, but lard or almond oil did not induce growth.

At the same time two other American workers,

McCollum and Davis, were making independent experiments upon rats to test the value of different salt mixtures in nutrition. The basal diet of these rats was—

Protein in the form of purified casein.

Fat in the form of lard.

Carbohydrate in the form of lactose (milk sugar) and starch or dextrin.

Salts: the mixture to be tested.

On this artificial food-mixture young rats grew for about sixty to eighty days and then failed to make further growth. The rats resumed growth if an ether extract of egg or butter were given, but extracts of lard, cotton-seed oil, or of olive oil had no restorative effect.

The combined results of these two separate groups of workers proved that fats can be divided into two classes, which may be called good or bad for nutrition :—

Good Fats.	*Bad Fats.*
Butter.	Lard.
Cod-liver oil.	Almond oil.
Egg fat.	Olive oil.
Kidney fat.	Cotton-seed oil.

From these results it seemed as if the only essential growth-promoting substance were contained in the good fats, but neither the diet used by Osborne and Mendel nor that used by McCollum and Davis could be called absolutely " pure." Osborne and Mendel used protein-free milk instead of pure salts, and McCollum and Davis used a commercial preparation of lactose. McCollum, whilst carrying out some experiments with birds fed on white polished rice and suffering from polyneuritis, discovered that the polyneuritis could be cured by the addition of commercial lactose. This new discovery led McCollum and Davis to modify their basal diet for rats; they replaced the lactose by dextrin or starch, and found that no appreciable growth took place even with the inclusion of 5 per cent. butter fat in the diet. Similarly if the

protein-free milk in Osborne and Mendel's experimental diet were replaced by artificial salt mixtures the rats did

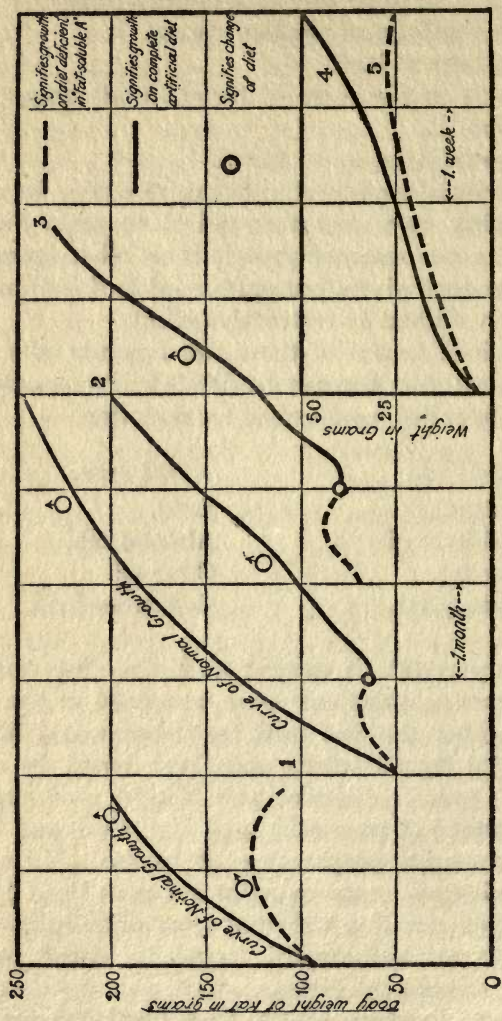

FIG. 10.

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not grow even if butter or egg fat were used instead of lard. The commercial lactose in one case and the protein-free milk in the other were thus supplying another

essential factor. Two substances, one soluble in water, the other in fat, were therefore necessary to secure growth and maintain health. McCollum named these two accessories "fat soluble A" and "water soluble B," as their chemical nature was unknown. They objected to the term "vitamine" introduced some years previously by Funk in connection with beriberi. They disliked it partly because it was not proved that the unknown substances were organic bases as the term "amine" implied, and partly because other organic substances, such as tryptophan (p. 105), are also essential for life. The term "accessory food factor" used by Hopkins was not considered satisfactory, as it suggested a subordinate rôle and might lead to a confusion with condiments. The word "vitamine" has, however, crept into general use and is now spelled "vitamin," the terminal *e* having been dropped, as it implied that the substances had a known chemical constitution.

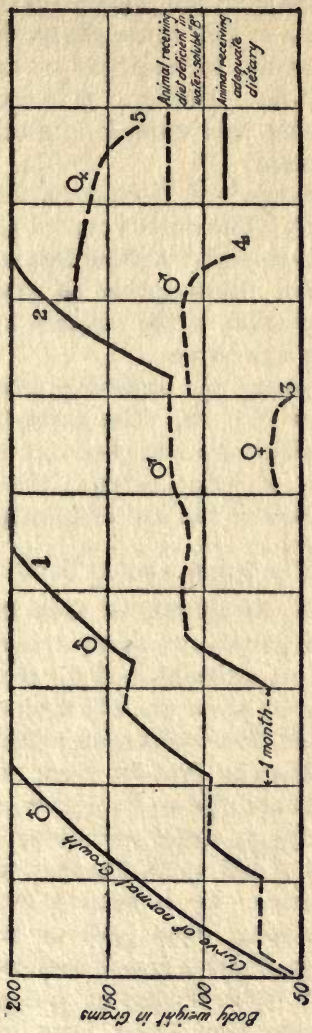


FIG. 11.

Reproduced by kind permission of the Controller of His Majesty's Stationery Office, from Report of Medical Research Committee on Present Knowledge Concerning Accessory Food Factors (Vitamins).

The absence of A-vitamin in a diet with the conse-

quent cessation of growth is shown in curves 1, 2 and 3 of Fig. 10. At the point marked o, A-factor (butter fat) was added to complete the diet, and growth was resumed. Curve 4 in this figure shows the normal growth of young rats nursed by mothers on an artificial diet containing butter fat. In curve 5 is seen the cessation of growth of young rats nursed by mothers on a diet deficient in A-vitamin.

The need of B-vitamin for growth is illustrated in Fig. 11. The dotted curves 3, 4, 5, and the dotted parts of curves 1 and 2 show loss of weight in absence of this vitamin. Resumption of growth immediately followed the addition of the vitamin as shown in the continuous line of the curve.

A young rat suffering from B-vitamin deficiency is seen in Fig. 12. The animal is unable to use its hind legs, which are stretched out in a helpless manner. After a dose of yeast extract, the animal was able to walk with ease at the end of twenty-four hours.

The Need for a Third Accessory Factor.

Rats, on account of their small size, are a convenient animal for laboratory experiments. It is possible to prepare sufficient artificial food for their use for long periods, and they soon show the effect of any inadequacy in the diet. Further, their short span of life, about three years, enables records to be kept for more than one generation.

Rats are able to live, grow, reproduce and rear healthy offspring on a diet containing purified protein, fat, carbohydrate and salts, together with some source of A and B factors. Upon such a diet man would get scurvy unless some fresh fruit or vegetables were also given. This peculiarity is not confined to man but shared with several other species of animals. Guinea-pigs, monkeys and also pigs suffer from scurvy, and Captain Cook recorded symptoms of scurvy in goats and sheep after several months on board ship. Rats, cats, rabbits and birds show no visible signs of scurvy.

The antiscorbutic substance is now included amongst the vitamins, and is called " water soluble C." The three

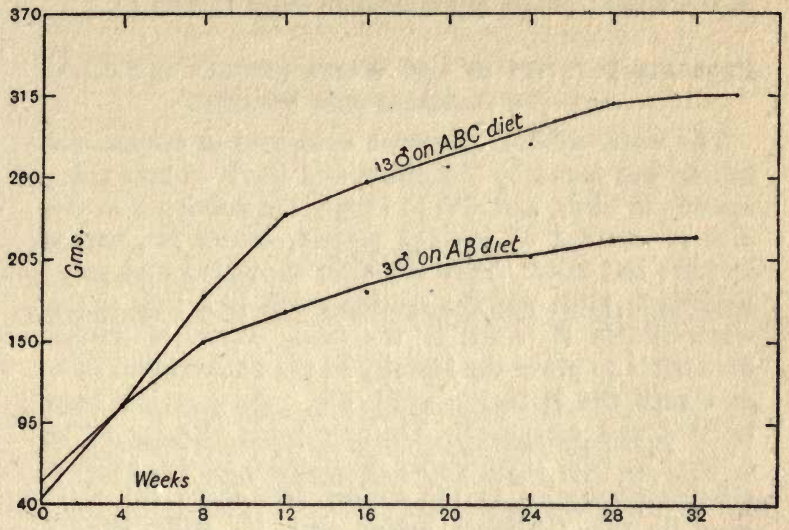


FIG. 13.—Weight charts of two male rats on diets containing A-, B-, and C-Vitamins and A- and B-Vitamins respectively.

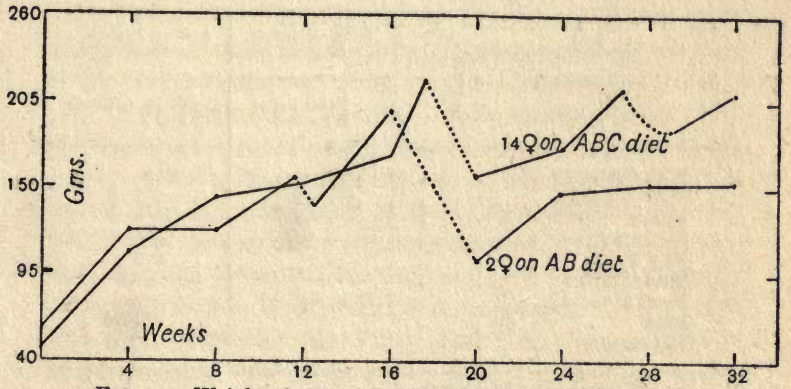


FIG. 14.—Weight charts of two female rats on similar diets. (Harden and Zilva.)

Reproduced by kind permission from the *Biochemical Journal*, 1918, **12**, 414 (Cambridge University Press).

vitamins are often called A, B, and C factors. All three factors are really essential for perfect growth and main-

tenance; even rats grow better if the C factor is added to their basal diet as well as A and B factors; this is shown in the weight charts reproduced in Figs. 13 and 14.

Probable Identity of the Water-soluble B Factor and the Antiberi-beri Vitamin.

The water-soluble substance contained in commercial lactose was found by McCollum and Davis to cure polyneuritis in birds, and also to supply the deficiency in the diet of rats fed on purified protein, butter fat, carbohydrate and salts. They therefore concluded that polyneuritis in birds was the specific result of a lack of the water-soluble B factor in the food. It is, of course, impossible to prove the identity of the antiberi-beri vitamin with the B factor until the substance has been isolated and compared. Their probable identity is indicated by their very similar distribution as well as their relative proportion in the various food-stuffs (which is seen in the following table), and by their similar properties.

Foodstuff.	B Factor tested on Rats.	Antiberi-beri Factor tested on Birds.
	Value for B Factor.	Value for Antiberi-beri Vitamin.
Rice Germ	+++	++++
Wheat Germ	+++	+++
Yeast	+++	+++
Ox Liver	++	+++
Egg Yolk	++	+++
Wheat Bran	+	++
Meat Muscle	+	+
Milk	+	slight
Potatoes	+	slight
Commercial Meat Extract Tinned Meat White Bread White Flour Polished Rice.	Both Factors missing.	

The identity of these two factors is now generally accepted.

CHAPTER V

DISTRIBUTION OF THE VITAMINS AND QUANTITIES REQUIRED

B-Factor.

The observations of Eijkman and other investigators of beri-beri made possible a rough classification of food-stuffs into those preventing and those not preventing beri-beri (p. 24). Further knowledge was needed, and the work of standardising the antiberi-beri, or, as it is sometimes called, antineuritic, value of common food-stuffs was begun by Cooper at the Lister Institute in 1913, and extended in 1917 by Chick and Hume working at the same Institute. The pigeon was selected for the test bird, instead of the fowl, as it suffers sooner from beri-beri and is more easily cured. Two kinds of experiments, preventive and curative, were made. Pigeons fed on highly-milled rice without the addition of some protective food-stuff lose weight and develop severe symptoms of polyneuritis in 15 to 20 days, soon followed by complete paralysis and death. The preventive value was determined by making a series of experiments in which different known amounts, such as 0·5 grm., 1 grm., 2 grms., etc., were added. If at the end of 60 days the pigeons showed no signs of polyneuritis, protection was considered to be good. In the curative experiments the birds were fed with polished rice until severe symptoms developed; a measured quantity of some special food-

stuff was then given and the least amount required to effect a cure determined. A most remarkable feature of polyneuritis is the rapidity with which the paralysis disappears if it has been of only short duration.

The work of Chick and Hume was of an urgent character, for our armies in the East were suffering from beri-beri and a remedy was required immediately. Few of the foods tested by Cooper were practicable for army use in Mesopotamia, and of the many tested by Chick and Hume only one could be used. This was a special commercial preparation of yeast extract sold under the name of Marmite. It was found that 1·5 to 2 grms. of this extract rapidly cured a test bird. It was difficult to gauge the quantity required by man, but the maximum quantity of the yeast preparation available was reserved by the makers for the armies in the East, and a consignment was sent out every month. To ensure that the men actually ate their ration it was made up with pea-flour in the form of a tablet pleasantly flavoured, so that it could be eaten either dry or dissolved as soup. The presence of the antiberi-beri substance in many food-stuffs has also been tested by workers in America and the Philippines, but few of these tests were of a quantitative nature.

PROTECTIVE VALUE OF VARIOUS FOOD-STUFFS AGAINST POLYNEURITIS (BERI-BERI) IN A PIGEON.

Food-stuff.	Minimum Daily Ration to Prevent Polyneuritis.	Food-stuff.	Minimum Daily Ration to Prevent Polyneuritis.
Yeast Extract . .	1·0 grm.	Ox Heart Muscle .	5·0 grms.
Wheat Germ, free from bran . . .	1·5 grms.	Ox Brain . . .	6·0 ,,
Pressed Yeast . .	2·5 ,,	Sheep Brain . .	12·0 ,,
Lentils, whole .	3·0 ,,	Beef Muscle . .	20·0 ,,
Egg Yolk . . .	3·0 ,,		
Ox Liver . . .	3·0 ,,	Cow's Milk, more than	35 ,,
Barley, unhusked .	3·7 ,,	Wheat Bran, free from germ, more than .	2·5 ,,
Barley, husked .	5·0 ,,	Cheese, more than .	8·0 ,,
Peas	5·0 ,,	Fish Muscle, more than	10·0 ,,

Curative Dose for a Pigeon with Polyneuritis.

Food-stuff.	Dose.	Food-stuff.	Dose.
Rice Germ [1]	0·5–1·0 grms.	Dried Vegetables, commercial, alcohol extract	40 grms.
Yeast Extract	1·5–2·0 ,,	Egg Yolk (= 4 yolks)	60 ,,
Maize Germ	1·0–3·0 ,,	Fish Roe, hard, of Turbot, alcohol extract	70 ,,
Wheat Germ	2·5 ,,	Spring Greens, alcohol extract	120 ,,
Pressed Yeast	3·0–6·0 ,,	Raw Beef, alcohol extract	140 ,,
Malt Extract,[2] samples 1 and 2	5·0–7·0 ,,	Potatoes, alcohol extract	350 ,,
Dried Whole Egg	2·0 ,,		
Dried Lentils, alcohol extract	20·0 ,,		
Dried Peas	40 ,,		

Wheat Bran, stone-ground, contained some germ	5 grms., sometimes cured.
Wheat Bran, roller-milled, free from germ	5 ,, ,, ,,
Dried Dates, alcohol extract	26 ,, did not cure.
Malt Extract [2]	10 ,, ,, ,, ,,
Meat Extract, commercial sample	10 ,, ,, ,, ,,
"Maconochie Ration," alcohol ext.	440 ,, ,, ,, ,,
Potato Peelings	630 ,, ,, ,, ,,
Dried Currants, alcohol extract	60 ,, ,, ,, ,,

From the above data a useful table [3] has been compiled showing approximately the relative antiberi-beri value of some common natural food-stuffs (weight for weight); the value of wheat germ being taken as 100.

Food-stuff.	Antiberi-beri Value.	Percentage of Water.
Rice Germ	200	10–13
Wheat Germ	100	10–13
Lentils	80	—
Yeast, Pressed	60	70
Egg Yolk	50	70
Ox Liver	50	70
Peas, dried	40	12
Wheat Bran	25	10–13
Beef Muscle	11	75
Potatoes	4·3	80

The supply of the antiberi-beri substance in the diet of man is thus derived principally from seeds of plants and eggs of birds.

[1] The Rice Germ was picked out by hand from the unmilled grain in the laboratory, a most laborious process.

[2] Notice the different value for malt samples.

[3] Report of Medical Research Committee on Vitamins.

The quantity factor must also be considered from another standpoint. Birds kept without food but receiving water eventually die of starvation without any signs of polyneuritis; the period of survival in this case exceeds the average period in which polyneuritis develops on a diet of white polished rice. It would therefore appear that the antiberi-beri substance is required in greater amount while food is being taken in, digested and assimilated, and the functions of the body are in full activity. In other words, the requirement for this substance is proportional to the rate of metabolism. The work of Braddon and Cooper indicated that the amount of the antiberi-beri substance required is proportional to the total fuel value of the food, particularly to the amount of carbohydrate in the diet. McCarrison found the addition of butter injurious if the diet were deficient in B-factor. Plimmer and Rosedale found an increased amount of cod-liver oil in the diet of birds caused loss of appetite and loss of weight unless the amount of B-factor were increased proportionately.

C-Factor.

Scurvy became a serious hindrance to military operations in Mesopotamia, and an immediate appeal was made by the Army authorities to the scientific world. The utmost credit should be given to Miss Chick and her colleagues and to Professor Harden for their prompt help with practical suggestions and demonstrations to prove that what was known to scientific workers could be applied successfully. Laborious feeding experiments on animals were at once begun at the Lister Institute and carried through as quickly as possible, so as to form a standard of comparison of the antiscorbutic value of different food-stuffs. The traditional and official antiscorbutic remedy, preserved lime-juice, which had failed repeatedly in practice, also failed in experimental

tests upon guinea-pigs (see p. 151). Suitable alternatives were suggested; the most practicable for Army use was germinated pulse (peas, beans, lentils, etc.). The dry seeds could be sent any distance, kept for considerable periods and germinated as required; moreover, the Indian troops, who were the greatest sufferers from scurvy, were large eaters of pulse, so that it was a measure which could be adopted without involving any change in the food supply. Other seeds, such as wheat, barley and rye, were equally suitable for the purpose. The seeds, of course, must be in a natural condition, neither milled, decorticated nor split. The seeds were soaked in water for twenty-four hours and then kept moist with access of air for one to three days until they sprouted. Subsequent cooking must be for a short period, not more than twenty minutes.

The methods used at the Lister Institute were essentially the same as those of Holst and Fröhlich, but the animals were fed on a scorbutic diet of oats, bran and sterilised milk to which was added the food-stuff to be tested. The experiments of Chick and Hume were especially designed to determine the least daily quantity of various foods required to maintain health and prevent scurvy. Since the quantities were quite unknown at the start, numerous experiments had to be carried out at the same time. For instance, in order to test the antiscorbutic value of cabbage on guinea-pigs, the animals were fed in groups on 1 grm., 2 grms., 5 grms. and 10 grms. respectively of cabbage daily in addition to the basal diet. The animals were kept separately so as to be certain that the special food was all taken, and if necessary it was given by hand. Scorbutic symptoms on the basal diet alone usually appeared about the twentieth day, followed by a rapid decline and death about the thirtieth day. If the addition of a special food-stuff prevented the appearance of symptoms for 90 days, a period three times the fatal period, it was considered to give complete protection.

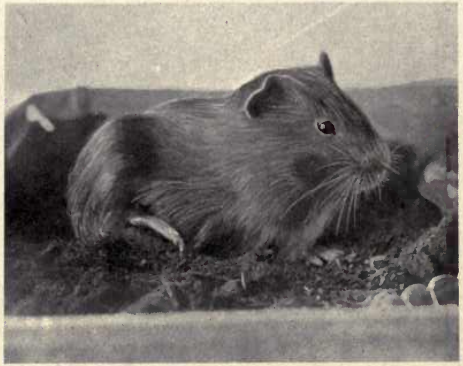
The symptoms of scurvy in guinea-pigs are tenderness and swelling of the joints due to hæmorrhages. The animals avoid unnecessary movement and assume unnatural postures, such as lying on the side with a painful limb held twitching in the air (Fig. 15). The teeth become so loose that hard food cannot be eaten. If partial protection is given by the test food-stuff, the animal may live long in this condition, recovering slightly from the initial decline in weight and depression of spirits. Post-mortem examination of guinea-pigs which have died of scurvy, show many features resembling the disease in man; hæmorrhages may be seen in any part of the body, especially in the limbs and intestine; the ribs and long bones are often swollen and fractured.

Individual variations in susceptibility are always found; 1 grm. of raw cabbage daily may be sufficient to protect most guinea-pigs, yet a few show signs of scurvy on this amount. The smallest daily quantity which ensures health is termed the minimal daily quantity. This quantity gives a standard of comparison for the antiscorbutic value of different foods. The minimal quantity required by a guinea-pig gives no indication of the daily quantity needed by man. Budd has related that sailors on a voyage to Madras in 1794, which took six months, had a ration of two-thirds oz. of lemon-juice every day; a few men showed signs of scurvy, but this disappeared on increasing the quantity. The Navy ration, issued in 1840, of 1 oz. of lemon-juice daily afforded complete protection. The minimal daily dose for man is thus about 1 oz. of lemon-juice daily. It is therefore possible to translate the minimal daily quantities of various food-stuffs required to prevent scurvy in guinea-pigs into the corresponding values for man by the use of simple proportion.

The minimal daily quantity of lemon-juice for the guinea-pig is 1·5 c.c., and of cabbage boiled for one hour is 5 grms.; the minimal daily quantity of lemon-juice for a man is 1 oz.; he would therefore require 3·3 oz. of boiled cabbage daily. Data for other food-stuffs can be calculated in the same way, thus :—

a

b



c

d

FIG. 15.—Guinea-pigs suffering from scurvy showing painful limbs in *a*, *c*, "face-ache" position in *b*, *d* (Delf). Reproduced by kind permission from the *Biochemical Journal*, 1918, **12**, 444. (Cambridge University Press.)

PROTECTIVE VALUE OF VARIOUS FOOD-STUFFS AGAINST SCURVY.[1]

Food-stuff.	Minimal Daily Ration for Guinea-pigs, (tested by Chick and co-workers).	Man (calculated).	Monkey (tested directly).
Cabbage, raw	1·0 grm.	0·6 oz.	
Lemon-juice	1·5 c.c.	(1 *oz. known*)	
Orange-juice	1·5 „	1·0 oz.	1·5 c.c. (tested by Harden and Zilva).
Swede-Turnip juice	2·5 „	1·6 „	
Preserved Lemon-juice	5·0 „	3·3 „	
Germinated Lentils	5·0 grms.	3·3 „	
Germinated Peas	5·0 „	3·3 „	
Cooked Cabbage (boiled half-hour)	5·0 „	3·3 „	
Runner Beans, green pods	5·0 „	3·3 „	
Fresh Lime-juice	10 c.c.	6·6 „	
Carrot-juice	20 „	13·3 „	
Beetroot-juice	20 „	13·3 „	
Apple-juice	20 „	13·3 „	
Grape-juice	more than 20 „	13·3 „	
Bananas	20 grms.	13·3 „	
Raw Meat-juice	20 c.c.	13·3 „	
Potato	20 grms.	13·3 „	
Milk	100–150 c.c	about 3–5 pts.	100–150 c.c. (tested by Barnes and Hume).

The minimal daily quantity for a monkey has been tested in the case of orange-juice and of milk. It is curious that although there is a great difference in the size of a monkey and a guinea-pig, their daily requirement of the antiscorbutic substance is practically the same. They differ in the period the disease takes to develop on a scorbutic diet, fifteen to twenty days in the guinea-pig and two months in the monkey.

A-FACTOR.

The standardisation of food-stuffs containing A-factor has not been worked out with the same detail as in the case of B- and C-factors. Drummond, from experiments on feeding rats, has tabulated certain fats according to their approximate value in A-factor as compared with butter, to which he has assigned the value 10.

[1] These are the quantities required when there is no other antiscorbutic food-stuff in the diet. Allowance must be made for loss of antiscorbutic value if the food is cooked or if not absolutely fresh.

Animal Fats.

Butter, average sample, approximate value as source of A-factor	10
,, from grass-fed cow	10
,, from cow after two weeks' winter feeding	8
Cod-liver-oil, average sample	10
Beef fat, subcutaneous	6–8
Horse fat	6–8
Dog fat, subcutaneous	6–7
Pig fat, from round the kidney	5–6
,, ,, subcutaneous	1
,, ,, refined = lard	0
Mutton fat	2

Vegetable Oils.

Palm oil, very dark	3–4
Maize oil, bright yellow	2–3
Linseed oil	1–2
Cotton-seed oil	1
Peanut oil	1
Olive oil	0–1
Sésame oil	0

This system of classification cannot be regarded as very satisfactory. Butter is an unsuitable fat to take as a standard because it is so variable in its A-factor content. Cod-liver oil is here only assigned an equal value with butter, although crude cod-liver oil is found by experience to be far more potent than butter. Zilva and Miura estimated that cod-liver oil is 250 times richer in A-vitamin than butter. Other workers have confirmed the superior value of the butter and milk of grass-fed cows to that of artificially fed cows. The leaves of green plants have been shown to be rich in A-factor. It appears to be formed in green tissues. Seeds and fruits contain small amounts. See Appendix. In general Drummond has shown that animal fats contain much more A-factor than oils prepared from the seeds of plants; the amount of A-factor in animal fats varies with the food of the animal, and the amount in vegetable oils varies with the method of refining.

CHAPTER VI

CHEMISTRY AND PHYSICAL PROPERTIES OF VITAMINS

B-Factor.

Little success has been obtained in the attempts made to isolate the antiberi-beri substance. Fraser and Stanton by chemical analyses of polished and unpolished rice hoped to get some clue as to the nature of the substance. They found that more phosphorus was contained in the whole grain (0·54 per cent.) than in the polished rice (0·26 per cent.), but the difference was insufficient to be a sure guide, as it varied in the several samples. They expressly stated that no significance should be attached to this observation. Schaumann, however, believed that beri-beri was caused by the absence of some organic phosphorus compound from the food. Feeding experiments with isolated organic phosphorus compounds have shown that this group of compounds has no curative action upon beri-beri. Funk cured fowls suffering from polyneuritis with a preparation which contained no trace of phosphorus, thus proving that the unknown substance is not a phosphorus compound.

At one time it seemed as if Funk had actually isolated the antiberi-beri substance; he obtained a small quantity of an active crystalline compound from rice polishings, yeast, dried milk, ox-brain and lime-juice. The difficulties confronting the chemist are really very great. The substance exists in minute quantities in food-stuffs, hence very large quantities of material must be taken at the start. In the absence of knowledge of the chemical properties of the substance every stage in the process

must be tested upon birds to see if the active substance be still present. In his first attempt Funk used 54 kilos (= 120 lbs.) of rice polishings, which he worked up in portions of 1·5 kilos with 4 litres (= 7 pints) of acid alcohol. The total extract amounted to some 126 litres (= 25 gallons). This large quantity of liquid had to be carefully evaporated *in vacuo;* a residue weighing 347 grams (= 12 oz.) consisting mainly of fat was obtained; it was treated with water and ether to remove fat and the volume of watery liquid became 17 litres. From this 17 litres of liquid one dose, corresponding to 20 grms. of the original rice polishings, was required to cure polyneuritis in pigeons. Further lengthy and laborious operations gave a solution of which a dose equivalent to 40 grms. of the original rice polishings was required to effect a cure. Thus loss occurs at each stage. Eventually from all this bulk of material Funk obtained a precious 0·5 grm. (= 0·02 oz.) of substance, just enough to test on birds and analyse. A single dose containing 172 milligrams (= 0·006 oz.) of the substance was sufficient to cure a pigeon with polyneuritis. The analysis of the substance gave a formula $C_{17}H_{13}O_4N$. Nothing was left after this analysis and curative experiments had been made. The substance was believed to be an amine, that is a nitrogenous base, and was called by Funk *vitamine.*

Funk still persisted in this laborious work, and used even larger amounts of rice polishings, yeast, milk and other foods, but never got further than with the first experiment, except that he eventually found his vitamine was not a pure chemical substance but a mixture of impurities. Only a very small quantity of the pure substance can be present in the original food-stuffs. Workers outside bio-chemical laboratories hardly appreciate the labour involved in such an operation and the resulting disappointment.

The chemists' difficulties are enhanced by the instability of the vitamins to heat, chemical reagents, oxidation,

drying, etc. Of the three known vitamins B-factor is by far the most stable. It is not destroyed by drying, and dry seeds retain this vitamin for long periods. Heating to 100° C. is not harmful, but it is destroyed by heating to 115 to 120° C. under pressure for several hours.

B-factor is soluble in dilute alcohol, but only slightly soluble in absolute alcohol, chloroform, ether, benzene and acetone.

It is not easily destroyed by acid, and is extracted from rice polishings, etc., with acid alcohol. Funk stated that this vitamin withstood hydrolysis with 20 per cent. sulphuric acid for six to ten hours, but Drummond found that the antineuritic value of marmite was greatly diminished by heating for ten hours with 20 per cent. sulphuric acid.

B-factor is more sensitive to the action of alkali, and loss takes place on working with it in alkaline solutions. The rate of destruction is slow at room temperature, but heating with 5 per cent. caustic soda for five hours caused complete destruction. Experiments made by Daniels and McClurg on the cooking of beans indicate that the addition of soda as commonly used in cooking does not appreciably diminish the amount of this vitamin.

B-factor is adsorbed and carried down by any precipitate, or by any finely divided powder, present in a solution; this is a troublesome property from the chemist's point of view in attempts to isolate the pure substance. Harden and Zilva showed that the antineuritic factor in yeast extract is completely adsorbed by a pure preparation of fullers' earth, known as Lloyd's reagent. This powder can thus be made an active source of B-vitamin; the fullers' earth is quite harmless and does not pass through the wall of the gut, but the B-vitamin is assimilated. Fullers' earth activated by B-factor is a convenient form in which to administer concentrated doses of B-vitamin. Eddy has used with good effect an activated preparation of fullers' earth in the treatment

of marasmic infants: 1 grm. of this powder contained the B-factor from 54 grms. of fresh lamb's pancreas.

On treating a mixture of equal volumes of autolysed yeast and orange-juice with fullers' earth, the B-factor is removed and the anti-scorbutic activity of the solution undiminished. By this means it is therefore possible to separate B-factor from C-factor.

B-factor is destroyed by radium emanations, but is not destroyed by ultra-violet light.

C-Factor.

The isolation of the antiscorbutic substance presents even greater difficulties to the chemist than the antiberiberi substance, as it is more easily destroyed by oxidation, heating, drying and other processes.

The action of heat upon the antiscorbutic value of vegetables and fruit-juices has been carefully studied by Miss Delf at the Lister Institute :—

Cabbage-leaf heated in water [1]—					
at 60° C.	for one hour	loses	70	per cent.	of its value
at 70–80° C.	for ,,	,,	90	,,	,, ,,
at 90° C.	for 20 minutes	,,	70	,,	,, ,,
Cabbage juice heated—					
at 100° C.	for one hour	loses	80	,,	,, ,,
Swede-turnip juice heated—					
at 100° C.	for one hour	loses	50	,,	,, ,,
Orange juice and lemon juice heated—					
at 110° C.		no apparent loss.			

Hess and other observers have also found that the antiscorbutic value of orange-juice is not diminished by boiling for short periods. Hess has used successfully the juice of canned tomatoes in the prevention of infantile scurvy, so that tomato-juice must also be relatively stable to heat. On the other hand, the antiscorbutic substance in milk is very easily destroyed by heating. Like vegetables, milk suffers less loss of this factor on boiling for a few minutes than by gentle heating for longer periods. Hess and Fish reported cases of scurvy in New York in infants following the use of milk pasteurised at 145° F.

[1] 100° C. or 212° Fahr. is the boiling point of water.

for thirty minutes; the infants were cured by substituting unheated milk for the pasteurised milk. In Berlin, an outbreak of scurvy was traced to the instalment of a pasteurising plant by one of the largest dairies; the pasteurisation was discontinued and the number of cases of scurvy decreased as suddenly as it had increased. The antiscorbutic value of milk is reduced but not entirely destroyed by pasteurisation; milk commercially pasteurised is usually re-heated in the home and the C-vitamin is completely destroyed by the second heating.

The sensitiveness of the antiscorbutic substance to heat varies according to the medium in which it is contained. Orange-juice and tomato-juice are much more acid than cabbage or milk, but the addition of citric acid to the water in which cabbage is boiled does not lessen the destruction of this vitamin. Hence acidity is not the protective agent against destruction; it is possible that the varying sensitiveness to heat is in some way connected with the amount and nature of the protein in solution.

C-factor is rapidly destroyed by alkali, such as common washing soda, sodium bicarbonate or the alkaline citrates. The destruction is particularly rapid if heat is applied at the same time; hence the practice of boiling green vegetables with soda to improve their colour is greatly to be condemned. The preparation of infants' foods by adding sodium or potassium carbonate to the milk mixture has proved to be productive of infantile scurvy. Faber has shown that the antiscorbutic value of milk is seriously reduced by the addition of 0·25 per cent. of sodium citrate. A case of severe scurvy has been recorded in a child of ten months fed from birth on raw milk to which sodium citrate has been added in the proportion of one grain to each ounce of the milk mixture.

C-vitamin disappears during the ageing of food-stuffs. Harden and Zilva and also Hess have shown that lemon-juice and orange-juice kept in a cold store for a fortnight diminish in antiscorbutic value. Milk, especially pasteur-

ised milk, deteriorates very rapidly, but the loss of value in sour milk proceeds more slowly. Although vegetables air-dried in the ordinary way are useless as antiscorbutics, certain food-stuffs dried with special care retain their potency, and ageing has less effect upon them in the dry condition. Lemon and orange juice dried *in vacuo* by Harden and Robison were found to be still active after careful storage for two years. Dry and stable forms of orange-juice should therefore be available in the future in a form suitable for use on long expeditions.

Orange-juice can be dried by the same commercial processes as are used for drying milk, but these preparations are not as active as those dried *in vacuo*. A dry preparation of specially neutralised lemon-juice, made by Harden and Zilva, had a wonderful effect upon a bad case of infantile scurvy in which the action of ordinary orange-juice was too slow; a quantity equivalent to the juice of nine lemons was given in one day, and the child then made rapid improvement.

Desiccation of cabbage in an atmosphere of carbon-dioxide for thirty-five hours at 65° C. did not prevent the destruction of C-factor. Cabbage has been successfully dried by a special process devised by Holst and Fröhlich; the preparation retained much of its efficacy after storing for twenty-six months at tropical temperatures in evacuated bottles. They hoped that cabbage preserved in this way might be a practicable form of antiscorbutic for use on Norwegian sailing ships. The investigations of Shorten and Ray show that mixed vegetables dried in a factory have no antiscorbutic value, but sun-dried potatoes, tomatoes and cabbage retain some of their potency. Spinach, turnips, turnip-tops and carrots sun-dried in the same way lost all their antiscorbutic value. Milk dried by certain commercial processes retains much of its antiscorbutic value.

The destruction of the C-vitamin during heating, ageing and drying may be partly due to oxidation. Some of the C-factor in milk is destroyed by bubbling air

through it, but the destruction is greater if more active oxidising agents, such as oxygen itself or hydrogen peroxide, are used. Hess has found by experience with infants that milk loses much of its antiscorbutic value by excessive handling during transit from the cow to the baby. Many of the processes used in dairies involve the exposure of large surfaces of milk to air, and frequent passage from one container to another is practically equivalent to the bubbling of air through milk.

The antiscorbutic value of foods is not necessarily destroyed by fermentation. Guinea-pigs are protected from scurvy by the same-sized dose of fermented lemon-juice as of unfermented juice. Cider, and alcoholic liquors prepared from freshly germinated grain, if used in large quantities, are instrumental in curing and preventing scurvy. Stefansson, the Arctic explorer, mentions the cure of scurvy in three days in men who found a dead musk-ox and ate its very rotten flesh. Eskimos, he reports, often live for months on putrid meats and fish without getting scurvy. In the old days sauerkraut (fermented cabbage) had a great reputation as an antiscorbutic; in particular, the relative freedom from scurvy of the Dutch sailors was attributed to the liberal use of sauerkraut. Possibly it is now prepared by a different process, for Ellis and his co-workers have recently tested sauerkraut as used in the States and found it to have no antiscorbutic value. Silage prepared from corn (the green leaves and stems) also was valueless, but as the silage during the process of fermentation may rise to a temperature of 30° C. for a month or more, heat rather than actual fermentation may be the destructive agent.

The antiscorbutic substance has been shown by Zilva to be unaffected by exposure to ultra-violet light.

A-Factor.

This vitamin, usually associated with fats, is not a fat. Fats are saponified (converted into soaps) by treatment with alkali, but A-factor in butter is not destroyed by

boiling with 20 per cent. alcoholic potash for half an hour (Steenbock, Sell and Buell).

The distribution of A-factor and of the yellow pigments in fats often runs so parallel that it was suggested that the A-factor might be identical with the yellow pigments called lipochromes in animals and carotinoids in plants. Both A-factor and yellow pigment in animal fat are derived ultimately from plant tissues and not synthesised in the animal body. Tomatoes, which are rich in pigment, were also shown by Osborne and Mendel to be rich in A-factor. Drummond tried feeding experiments with carotene; neither impure nor pure crystalline preparations improved the condition of animals suffering from a deficiency of vitamin. It has also been shown that cod-liver oil, dog fat, the kidney fat of pigs and other fats are poor in pigment and yet disproportionately rich in A-vitamin. Miss Stephenson has shown that butter fat can be decolorised without impairing its vitamin value. Much other evidence has also been brought forward to disprove the identity of A-factor and carotene; the substances are not even quantitatively associated in the very plant tissues in which they are most probably synthesised.

The recorded observations on the effect of heat upon A-factor were at first very discordant, but now it is generally agreed that the rate of destruction varies with the exposure to oxidation during the heating process. Hopkins found that A-factor in butter is resistant to heat alone up to a temperature of about 120° C., but is rapidly destroyed if air is bubbled through the melted butter during heating. The substance is therefore decomposed by atmospheric oxygen. The A-vitamin in milk, green vegetables, grain and carrots, etc., is not destroyed by heating in an autoclave for three hours at 15 lbs. pressure (about 110° C.).

A-factor is not easily destroyed by ageing; it suffers little loss if protected from oxidation. It is not destroyed in the process of making silage from green fodder.

The A-vitamin is completely destroyed by the process of hardening oil by the action of hydrogen, as in the manufacture of margarine from oils.

Zilva has shown that butter is inactivated by exposure in thin layers to the action of ultra-violet light for five to eight hours, probably by the ozone produced by the action of the mercury-quartz lamp upon atmospheric oxygen. The potency of cod-liver oil is destroyed by the action of ozone more rapidly than by the action of oxygen.

This vitamin is soluble in alcohol, ether or benzene. Osborne and Mendel made a very active ether extract of dried green leaves; 30 milligrams (0·001 oz.) of extract per day supplied sufficient A-vitamin for rats.

Drummond has shown that the amount of A-factor in seeds is not increased by germination. A-factor is synthesised in the green parts of the plant, and the white leaves of cabbage contain less A-factor than the green leaves. Lower plants (marine algæ) containing chlorophyll synthesise this vitamin. The marine algæ are eaten by small marine animals which in turn are eaten by bigger ones, eventually by codfish. The A-factor in the codfish is chiefly concentrated in its liver.

CHAPTER VII

RICKETS AND A DEFICIENCY OF THE FAT-SOLUBLE A-VITAMIN?

THE discovery of the indispensability of the fat-soluble vitamin for the growth of rats, together with the well-known curative action upon rickets of cod-liver oil, milk, butter and eggs, food-stuffs rich in this vitamin, gave rise to the theory that rickets might be connected with an insufficiency of this factor in the food. Both Hopkins and Funk suggested that rickets, like beri-beri and scurvy, was the result of a specific deficiency in the diet. Hopkins first acquired a bias in favour of a dietetic factor in the causation of rickets by observing in Venice that this disease was most frequent in families who never used dairy products of any kind. This view is strengthened by the conclusion of Drs. Cheadle and Poynton from their clinical experience with rickets. Before the conception of accessory food factors was formulated, they wrote:[1]

"Rickets is produced as certainly by a rachitic diet as scurvy by a scorbutic diet. Children of well-to-do parents, under hygienic conditions so far as air, light, cleanliness and warmth are concerned, get rickets if the diet is at fault. Such cases are cured in fact by an antirachitic diet as certainly as scurvy by an antiscorbutic diet. The fault is of quality, not quantity. A child may be reduced by starvation to the last stage of atrophy and yet not be rickety. Conversely, it may be over-fed, fat and gross and yet be extremely rickety."

The known facts concerning the disease of rickets can now be reviewed in a new light, and it will be seen how they fit in with the theory that rickets is the result of a diet containing an insufficiency of the A-vitamin in a form available for the use of the infant.

[1] In Allbutt and Rolleston's *System of Medicine*.

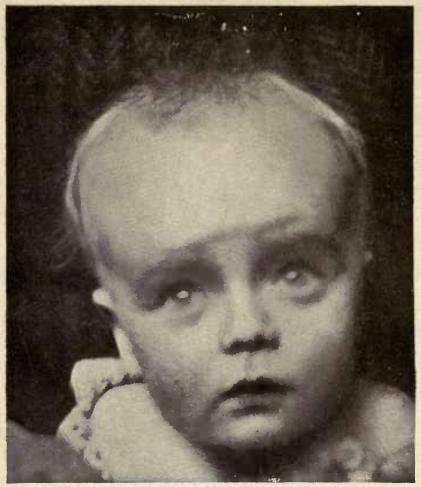


FIG. 16.—Front View.

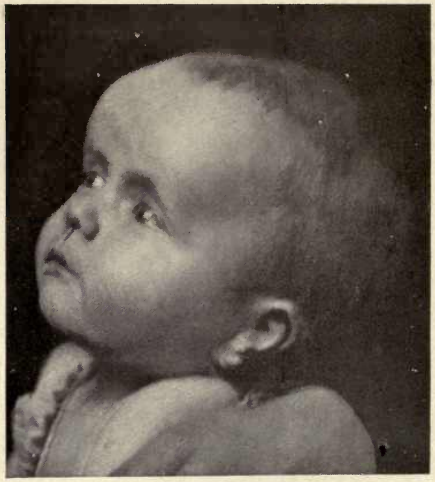


FIG. 17.—Side View.

Deformity of Child's Skull in Rickets.

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The havoc caused by rickets is more widespread than is generally realised. The cases with obvious bone deformity are only a small proportion of all those affected. The statistical figures of Lawson Dick in London and of Schmorl in Germany are appalling. Schmorl, from microscopical examination of the bones and of other organs of children dying under four years of age, found that 90 per cent. had rickets. Lawson Dick found that 80 per cent. of the children in some London County Council schools were affected. Another set of figures is very striking. The infant death-rate in the west of Ireland is only 30 per thousand, but in poor urban districts in Great Britain from 100 to 300 per thousand; rickets in the west of Ireland is practically unknown, but in the slums of English and Scottish towns it is very prevalent.

Symptoms.—Rickets is not merely a disease of the bones; the health, growth and development of the whole body is affected. It is seldom observed before the child is six months old, and is most active between the ninth and twenty-fourth months. A child, previously thriving and often growing particularly fast, becomes whining and restless, is disinclined for any exertion, and in severe cases may make no attempt to sit, walk or stand. The head enlarges and becomes flat and square on top with bulging sides as shown in Figs. 16 and 17. Only about 20 per cent. of these children look badly nourished; more often they are flabbily fat. The bones grow irregularly and remain soft and cartilaginous, leading in bad cases to permanent distortions and deformities, such as bow legs and knock knees. At the junction between the bones and cartilages of the ribs there is a thickening which gives rise to the condition known as the rickety rosary or beading of the ribs (cf. Scurvy, p. 36). The ends of the long bones enlarge, most obviously at the wrists and ankles. As the disease progresses the chest wall is distorted; it becomes narrow and depressed under the arm-pits, greatly reducing the chest cavity. Lung and heart troubles are caused by the pressure of the misshapen chest. The muscles are wasted and ligaments are soft and lax; the child seems "double-jointed" and is able to place the limbs in queer positions. The limbs are not tender to touch, and if there is appreciable tenderness a complication with scurvy should be suspected. Rounding of the spine is produced by muscular weakness; if placed in a

sitting position the child may sink in a heap. The disordered state of the whole body has its effect upon the nervous system; various forms of spasm and convulsion (tetany) are easily excited. Digestive troubles frequently, but not invariably, accompany rickets and the abdomen is distended. Sweating of the head is often observed.

Although generally associated with infancy and early childhood, rickets has been observed at a much later age. Late rickets, as it is called in older children, was a rare disease, but since the War it has become quite common in Central Europe, especially in Vienna. Late rickets does not respond to treatment with cod-liver oil so quickly as in infants.

Central Europe is now afflicted with rickets to a greater extent and in severer forms than ever before experienced in breast-fed and artificially fed infants. In one Austrian community rickets was diagnosed in 100 per cent. of the infants of nine months. It occurs in infants at a much earlier age than usual, and amongst older children there is much dwarfism and deformity. In Germany since 1917 there has been a marked increase of rickets showing all grades of deformity; 10 per cent. of the children of three to five years of age cannot walk, and it is likely that a considerable proportion of these children will eventually become a burden upon the State.

Rickets is seldom directly fatal, but children suffering from this disease are more easily attacked by broncho-pneumonia, tuberculosis and other infectious diseases. Whooping-cough, measles and bronchitis are far more grave if the child is rickety. Either sex is equally affected, but the consequences are far more serious for the female, as the contracted pelvis, a frequent result of rickets, makes childbirth difficult. The rachitic child also carries a stigma throughout life in the form of defective teeth. These children suffer more frequently from adenoids and enlarged tonsils. Lawson Dick found 66 per cent. had both adenoids and enlarged tonsils; 14 per cent. had enlarged tonsils alone; and 20 per cent. had adenoids alone.

Since Glisson first described this disease in his famous *Treatise on the Rickets* nearly 300 years ago, it has continually increased in spite of numerous theories and investigations as to its cause. It is now generally agreed that the prevention of rickets is fundamentally a dietetic problem. Dr. Still has classified the diets associated with the development of rickets:

(1) Very starchy food, such as bread, potato, biscuits, or cornflour with little milk.
(2) Excessively diluted cow's milk, whether fresh, condensed, or dried.
(3) Patent cereal foods.
(4) Breast milk supplemented by starchy food.
(5) Breast milk alone.

If one particular fault in the food is the cause of rickets it must be common to all these diets.

Excess of carbohydrate cannot be the essential factor, since diluted cow's milk and poor human milk without any added carbohydrate are included amongst the diets associated with rickets.

Insufficient protein is not the cause, since rickets occurs on diets 2, 4, and 5, which are not necessarily deficient in protein, for cow's milk diluted with an equal volume of water contains as much protein as human milk. Again, experiences at the London Zoological Gardens have proved that insufficient protein is not the cause; lion cubs weaned early and fed on a high protein diet of raw, lean meat became so rickety that they could not be reared.

An insufficient quantity of fat is common to diets 1, 2 and 3, and possibly to 4 and 5, but in rare cases rickets occurs if cream, making 6 to 7 per cent. of fat, is added to a milk mixture; after gaining well for a time such infants eventually suffer from disordered digestion, the fat is not assimilated and rickets occurs.

To whatever defect in diet or hygiene rickets is ascribed,

there is one cure which is so generally successful that it may be regarded as a specific, namely cod-liver oil.[1] The value of cod-liver oil in the treatment of this disease in infants has long been known, and at the suggestion of Bland-Sutton the rickety lion cubs at the Zoo were treated and cured by cod-liver oil. Other substances which have proved of value both in prevention and cure, but to a lesser degree, are butter, cream, eggs and milk. All these substances are fatty foods rich in A-vitamin (pp. 49, 62). This particular constituent of the fat is lacking in those diets associated with rickets except in the special case of over-feeding with fat.

A study of the social and economic factors in the causation of rickets, carried out in the city of Glasgow by Miss Ferguson, also showed the connection of rickets with a shortage of A-factor in the food, although this point was overlooked by Miss Ferguson. The non-rickety families had more milk, meat, margarine, fish, eggs and cheese than the rickety families, who used more flour, potatoes, sugar and oatmeal.

Fresh cases of rickets occur most frequently in the spring. In the United States twice as many occur from January to June as in the other half of the year; similar reports come from Great Britain and Germany. This seasonal variation in the incidence corresponds with the seasonal variation of cow's milk in respect to its content of A-vitamin. It has been shown by Drummond that the milk from a grass-fed cow is richer in A-factor than the milk from the same cow after several weeks of winter feeding. A-factor is of vegetable origin and is formed in the green parts of the plant. The feeding of cows in winter on straw and turnips, as is done in some districts,

[1] The value of cod-liver oil in A-vitamin is reduced by refining to remove the fishy taste, or by emulsification and admixture with other ingredients to make it more palatable. The crude oil has also been found to be the best in the treatment of rickets. A sample of cod-liver oil exhibited at a recent Sanitary Congress (1921) was described as "tasting like warmed-up pêche Melba"; the efficiency of such a pleasant preparation would probably be very slight, and it might have to be given in large quantities which would upset the digestion.

is likely to produce a milk very poor in this vitamin, as the green parts of the turnip are not eaten.

The antirachitic value of milk thus depends on the diet of the animal. In the same way breast-fed babies may receive milk lacking in A-vitamin if the mother's diet is poor in this respect. This fact is illustrated by statistics from New York: in a certain poor quarter 90 to 100 per cent. of the negro babies suffer from rickets, though almost all are breast-fed; the mother's food was found to be lacking in good fats and in green vegetables. A generation earlier the parents of these negroes lived in the West Indies on an entirely different diet of fresh natural food-stuffs; rickets amongst them was unknown.

Cheadle and Poynton only observed rickets to occur on a diet containing plenty of milk if loss of food had been caused by vomiting or diarrhœa. The rare cases occurring on an apparently ideal diet are traceable to the same cause; digestive disturbance, though not always obvious, may prevent the assimilation of A-factor as contained in butter or milk fat. All these cases respond to treatment with cod-liver oil, probably because oily fats like cod-liver oil are better assimilated than a hard fat like butter fat, and also because cod-liver oil has been estimated as being approximately 250 times richer than butter fat in A-vitamin. A-factor given in spinach has no power to alleviate rickets in infants because it passes through the intestine practically unaltered even when given in a finely-sieved form. The A-vitamin is of no use to the infant if offered in a medium which it cannot digest. Scurvy and rickets are frequently associated in the same child. It is now clear that the lack of either B-factor or C-factor or good protein in the food causes digestive trouble. A diet deficient in any of these ways, either singly or collectively, is therefore likely to prevent the assimilation of fat. Rickets in such cases may be of secondary origin; that is, not the direct result of food lacking in A-factor, but inability to utilise the good fats supplied. Feeding experiments on birds by Plimmer and

Rosedale indicated that A-factor, given as cod-liver oil, was only effective if the food contained a good supply of B-factor; increasing the amount of cod-liver oil without simultaneously increasing the amount of B-factor actually caused loss of weight. For normal growth and the prevention of rickets the diet must therefore be properly balanced. An infant over-fed with cream on a diet deficient in other factors may thus get rickets. Conversely, it has been shown by Hess and Unger, that on a well-balanced diet containing a relatively small amount of A-vitamin slow-growing children did not develop rickets. The requirements of slow-growing children for this vitamin are apparently less than those of fast-growing children, and the diet used by Hess would probably not have prevented rickets in children growing at a normal rate. Rickets must be regarded as a disease accompanying growth and is not seen in atrophic conditions.

The poorly calcified bones of rickety children led to a belief that rickets is caused by the absence of calcium salts in the food, and that it can be cured or prevented by the use of lime water. An insufficiency of lime salts in the food of a growing child or animal certainly produces soft bones, but the condition is not identical with true rickets. There is seldom a shortage of calcium salts in the usual rachitic diets, for even diluted cow's milk contains sufficient. Lime salts in cow's milk are chiefly present as acid calcium phosphate, which becomes insoluble in alkaline digestive juices, and will therefore pass through the body unchanged and be of no use. The assimilation of calcium as calcium phosphate depends upon the presence of hydrochloric acid in the gastric juice, which converts the calcium phosphate into calcium chloride and phosphoric acid, two soluble substances, probably separately assimilated in the intestine. For the proper calcification of growing bones two conditions are necessary: sufficient calcium salts must be assimilated; the calcium salts after assimilation must be deposited in the bone. True rickets

develops independently of the supply of available calcium; it is caused by an inability to retain the calcium salts in the body. There may even be a negative calcium balance; that is, more calcium salts are excreted in the urine than are assimilated from the food. The administration of cod-liver oil, egg, butter, etc., enables the body, by some means not yet understood, to retain and deposit in the growing bones and teeth the assimilated lime salts and to use them for the general purposes of the body. Sufficient calcium must, of course, be present in the food, and a deficiency of calcium is only likely to occur on a largely cereal diet. True rickets develops independently of the supply of lime salts in the food and cannot be prevented or cured by the simple addition of lime salts.

Experimental Rickets.

Professor E. Mellanby has shown that the production of rickets in growing puppies can be controlled by the kind of fat in the food. His experiments were upon newly weaned puppies, five to eight weeks old, and continued to the age of six months. The animals were constantly examined by X-rays to detect imperfect calcification or malformation of the bones. The results of these experiments are capable of extension to the treatment of children. A basal diet was selected which was consistent with fairly good health and growth, and yet soon produced rickets. The diet consisted of—

250 to 350 c.c. separated milk.
Unlimited white bread.
5 to 10 grms. of yeast (for B-factor).
3 c.c. orange-juice (for C-factor).
1 to 2 grms. of common salt.
10 c.c. linseed oil.

The separated milk contains calcium salts and sufficient protein to supplement the poor protein of white bread.

It contains B- and C-factors and chlorides and is really only deficient in the A-vitamin. The development of rickets could be controlled by simply substituting other fats for linseed oil. Experiments were also made to determine the effect of extra lime salts, which were increased by doubling the quantity of separated milk or by adding pure lime salts. In neither case was the development of rickets prevented.

Mellanby found that he could roughly classify foodstuffs according to their power of preventing rickets:

Preventing Rickets.	Slight Preventive Action.	No Preventive Action.
Cod-liver oil.	Olive oil	White wheat bread.
Whole milk.	Peanut oil.	Oatmeal.
Butter.	Lard.	Rice.
	Cotton-seed oil.	Separated milk.
	Lean meat.	Yeast.
		Orange juice.
		Linseed oil.
		Vegetable margarine.
		Calcium phosphate (= lime salt).
		Sodium chloride.
		Milk protein.

The fats preventing rickets correspond to the good fats, and the fats not preventing rickets to the bad fats for A-vitamin (see p. 49).

Rickets developed soonest in the fastest growing puppies, and sometimes disappeared as the puppies grew older without any change in the diet. These observations accord with the history of rickets in children; the disease is rare amongst wasted infants; it tends to accompany rapid growth; and may disappear spontaneously during the third year of life. The symptoms of rickets in puppies and children are alike. The puppies' bones are improperly calcified, the long bones are bent and the ends enlarged (see Figs. 18 and 19). The rickety puppy is lethargic and seldom barks or plays, just as the rickety child does not shout or play. Rickety puppies are more easily affected by distemper, broncho-pneumonia and mange than puppies on a normal diet.

FIG. 18.—Severe rickets in puppy (Mellanby).

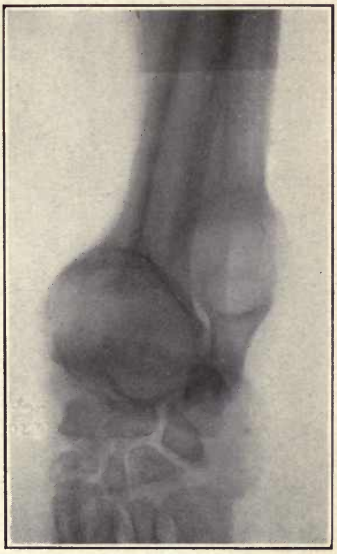

FIG. 19.—X-ray photograph of wrist-joint of same puppy (Mellanby).

Reproduced by kind permission from the *Lancet*, 1920, i, 860.

Exercise was found to delay the onset of rickets in poorly-fed puppies. Puppies kept in confinement on a "good" fat diet showed no signs of the disease. Confinement or lack of exercise are therefore only of secondary importance, contrary to the belief of Paton and Findlay of Glasgow, who still believe that any child or animal kept without exercise will develop rickets, however good the diet. As Mellanby has pointed out, if lack of exercise were the cause of rickets how easy it would be to stamp out the disease. It would be absurd to attribute the widespread epidemic of rickets in Central Europe following the War to any want of exercise; neither has there been any deterioration in the general hygienic conditions to account for this increase. The exercise of a healthy infant consists of a number of small movements carried out continually during waking hours; it could only be restricted in the infant by binding it hand and foot.

If rickets were produced by confinement in stuffy and insanitary rooms, the disease should be very prevalent in the island of Lewis in the Hebrides, where many of the people live in what are called "black houses," built with very thick walls of turf and stones with thatched roofs. There is often neither chimney nor window; the smoke from a continually burning peat fire has no outlet except by the door, which may open directly into the cow-byre; chickens have the run of the house and get on the beds, dressers and tables. The babies are seldom or never carried out, and remain in this atmosphere until they can run out by themselves. Yet the infant death-rate in Lewis is extraordinarily low, only about 40 per thousand as compared with 100 to 300 in large towns. Rickets is practically unknown in Lewis, and the inhabitants in general have perfect teeth, though presumably tooth-brushes are not in daily use. The common food-stuffs are fish, oatmeal and egg; the oily liver of the fish is a favourite dish mixed with oatmeal and milk and cooked in cod's heads, one head for each member of the family. The diet is thus rich in food containing A-vitamin.

During the course of Mellanby's experiments upon puppies, Mrs. Mellanby made a parallel series of observations on the effect of the various kinds of fat upon the development and health of the teeth. The animals had the basal diet already described (p. 79).

On the diet containing cod-liver oil, at the termination of the experiment (age about six months), all the " milk " teeth were changed and the permanent teeth developed in perfect condition.

On the diet containing butter, the results were not quite so good; at the end of six months some milk teeth still remained in the jaw, all the permanent teeth had not erupted and their enamel was slightly defective.

On the diet containing linseed oil, the change of teeth was still further delayed and the enamel was dark brown in colour.

It may be noted that in all cases the food was of a pappy consistency. The softness of our food is commonly blamed as the cause of defective teeth, but from these experiments the texture of the food appears to be of no importance. The conclusion was that good teeth were formed if the food contained cod-liver oil or butter, but that if the diet contained only food-stuffs poor in the antirachitic factor, there was delay in the shedding of the first teeth and in the formation of the permanent teeth. The diet affects the structure of the teeth from within, and they are then easily infected from the outside later.

Stefansson, the Arctic explorer, has stated that dental caries (decay) was practically unknown in Iceland before 1850. The diet then consisted chiefly of milk, mutton, fish, fowl, eggs of wild birds, carrageen moss and occasionally turnips and potatoes. Cereals and sugar (foods deficient in the A-factor) were introduced later, and since they have been in general use decayed teeth have become common. A similar deterioration was observed in the teeth of the Eskimos in Alaska when their original diet of meat and fat was replaced by cereals and canned foods.

We are almost forced to conclude that malnutrition in respect to the kind of fat is probably the primary cause of rickets and decayed teeth, and that the antirachitic property of certain fats is due to some still unknown chemical substance associated with them. There is evidence to suggest that the antirachitic substance is identical with the A-factor, and this view has been adopted by the Medical Research Committee in their Report, No. 38.

Rickets has been described in other species of animals. McCollum has observed signs of the disease in rats kept on a diet containing fat poor in the A-factor. Pigs are often said by farmers to be rickety; in some cases this condition in pigs is undoubtedly scurvy and responds to antiscorbutic treatment. An attempt by Golding, Drummond and Zilva to produce rickets in two young pigs fed from birth on a rachitic diet failed to produce typical symptoms. The animals did not grow normally; there was some beading of the ribs; one animal declined and died; the other declined, but health and normal growth were restored by the addition of cream to the diet.

Harden and Zilva kept three monkeys for several months on a diet poor in A-factor. No signs of rickets were observed, but as the animals were about two years old at the beginning of the experiment they were beyond the usual age for the appearance of this disease; the monkeys declined and died unless returned to a normal diet. Mackay fed kittens on a diet deficient only in A-factor. The kittens became very emaciated and died; there were no definite symptoms of rickets although there was some abnormality of bone formation at the rib junctions. The symptoms resembled those of cœliac disease in children, a condition in which there is a failure to digest fat, arrested growth, emaciation, distended abdomen and a hankering for food.

CHAPTER VIII

KERATOMALACIA (KERATITIS, XEROPHTHALMIA OR HIKAN) AND HUNGER-OSTEOMALACIA

RICKETS is not the only disease of malnutrition associated with the quality of the fat in the diet. Children on diets poor in "good" fats suffer sometimes from a purulent inflammation of the eye, which if unchecked leads to perforation of the cornea and blindness. This condition in infants and its relationship to malnutrition was first noticed by W. Mackenzie in 1857. In 1892 cases were recorded by Holmes Spicer amongst artificially fed children in England, and he also noted that the condition was not uncommon in countries where nursing mothers practised long fasts. In 1904 Mori observed 1511 cases of a disease, called Hikan, among Japanese children of two to five years, characterised by diarrhœa, excessive appetite, swelled abdomen, loss of weight, night-blindness, dryness of the skin and hair (cf. symptoms of Mackay's kittens, p. 83); 116 of these children developed keratomalacia. Most of them had been breast-fed for over a year, and afterwards their food consisted almost entirely of cereals and some vegetables. Mori found that the disease was cured by cod-liver oil, fish oils and chicken liver. Czerny and Keller (1906) described a nutritional disease in infants fed almost exclusively on carbohydrate; they called this condition "Mehlnährschaden," and keratomalacia was a common symptom. Ronne (1915) observed 35 cases of keratomalacia in Copenhagen in infants fed on buttermilk, During the two following years Bloch recorded 49 similar cases in Copenhagen. The sick infants were at first treated in the Eye Depart-

ment of the hospital without success. The children were all poorly developed, weak and anæmic, and some of the younger ones were greatly wasted. On inquiry, Bloch found that they had been fed on pasteurised, skimmed milk which had been re-heated in the home. Their food was therefore deficient in both the A- and C-vitamins, and they showed some signs of scurvy. Bloch ordered as much whole fresh milk and cod-liver oil as they could tolerate, thus supplying both the missing vitamins. Rapid recovery followed this treatment, but in those cases in which cod-liver oil was not given recovery was too slow to save the sight; an indication that the eye symptoms were caused by the absence of A-factor and relieved by its inclusion in the food. In the following year Bloch recorded still another outbreak of eye disease in an institution at Copenhagen. The younger infants and sick children were accommodated in one building and given whole milk; all these children did well. Thirty older children were housed separately in two sections. Their food consisted of gruels made of buttermilk, fruit syrups, barley, etc., fish, minced meat, potato, cocoa, bread and margarine; they had no butter, eggs, or cream. One of these sections had a little whole milk for breakfast, the chief source of A-vitamin, and the other did not. The children who had this small quantity of whole milk showed no symptoms and grew normally, but eight children in the section without whole milk were stationary or losing in weight; they showed signs of eye trouble which did not respond to local treatment and proved to be keratomalacia. No change was made in the general diet, but the eye trouble was cured in eight days by the addition of 10 grms. of cod-liver oil twice daily; the children also began to grow and improved in health. Bloch ascribed the effect of cod-liver oil to the presence in it of some unknown accessory substance. He called special attention to the frequent association of diarrhœa, bronchitis, pneumonia, pyuria, discharges from the nose and ear, and catarrhs of all sorts with the symptoms of

keratomalacia, evidently all due to lowered resistance to bacterial infection. No mention was made of rickets; but the children were stationary or losing weight, and rickets is a disease associated with rapid growth and rare in atrophic (wasted) infants or puppies.

A similar eye disease was observed during the War by Dr. Gideon Wells in Roumania, so severe as to cause blindness. These children had no milk, as the Austrians had taken away all the cows and their food was limited to corn-meal and bran and vegetable soup. To improve their diet under war conditions seemed impossible, but just at the most difficult time, Dr. Wells heard of a vessel putting into Archangel with a cargo of cod-liver oil. Through the agency of the Red Cross this cargo was sent to Roumania, where the oil saved the life and sight of many children.

Dr. Dalyell in her work among the famine-stricken children of Vienna came across cases of this eye disease in infants who had received little fat in their food; the symptoms disappeared on treatment with cod-liver oil.

In the Madras Presidency, according to Col. McCarrison, I.M.S., keratomalacia is common amongst ill-fed Indians, and is treated successfully by improved diet and cod-liver oil.

Budd in 1842, in his lectures on *Diseases arising from Defective Nutriment*, referred to ulcerated cornea; he recorded several cases which had arisen from a restricted diet following fever and were quickly healed under the influence of animal food.

Under ordinary conditions of life nutritional keratomalacia is a comparatively rare disease. Ross records only four cases among more than 28,000 infants admitted to the Johns Hopkins Hospital, Baltimore.

The connection between keratomalacia and a diet deficient in A-factor has been strengthened during the last few years by the experiences of scientific workers with rats fed upon artificial diets. Severe epidemics of eye disease have invariably occurred among rats fed on

diets deficient in A-vitamin. Other rats on a normal diet in close contact with those with the eye disease have remained healthy. McCollum and Davis (1917), who first described this affection in rats and called it xerophthalmia, believed it to be a deficiency disease. Eye disease in rats has been studied by Stephenson and Clark; a cure was effected in every case by the addition of food containing the A-vitamin to the diet. The actual inflammatory symptoms are produced by any bacteria, normally present in the eye, invading the corneal tissue. Guerrero and Conçepcion (1920) have observed eye disease followed by blindness in fowls fed on polished rice and extract of rice polishing to supply B-factor; this diet contained no A-factor.

Keratomalacia affords a remarkable example of lowered resistance to bacterial infection directly attributable to a specific dietetic deficiency. Two infantile diseases are thus associated with the absence or shortage of the A-vitamin in the food, and both are cured by its administration. There is no record of these two diseases appearing at the same time in the same individual. The explanation is suggested that keratomalacia is the result of an almost complete absence of A-vitamin over a short period, and that rickets is the result of a less complete deficiency of the vitamin over a longer period. The eye trouble is preceded by stoppage of growth and may be accompanied by wasting, while rickets most commonly occurs in a rapidly growing child.

Hunger-osteomalacia, or Hunger-malacia.

The bone disease osteomalacia in adults is now attributed to a diet deficient in A-vitamin. Towards the end of 1918 many cases of this bone disease were observed in Austria and Germany in adults suffering from food deprivation. The victims looked anæmic, old and ill, and had a dry, harsh skin. The most remarkable sign was the stiff, waddling gait with feet far apart; this

peculiar walk was adopted to avoid the acute pain caused by movement of the hip, knee, or foot joints. Stairs could not be ascended unless there was some support, so that the body could be hoisted by muscular effort of the arms. Pain was also caused by stooping. The muscles were not tender, but certain areas, always over bones, were very sensitive to pressure. In some cases there were spontaneous fractures of the bones. X-ray photographs showed osteoporosis. The symptoms were at their worst in winter and spring and less severe in the summer.

Hayer (1920) recorded that the disease in Munich was associated with a diet poor in energy value, and in fat, meat and fresh vegetables; it was cured by cod-liver oil containing phosphorus. In Vienna, Dalyell and Chick found that the diet in these cases consisted mainly of bread and vegetables with small amounts of flour and sugar; milk, butter and eggs had not been used on account of their prohibitive price; lard, the only kind of fat, was not always obtainable. The patients were cured by rest in bed and good food. The dietetic origin of the disease was thus confirmed. A careful investigation was made by Dalyell and Chick and by Hume and Nirenstein to determine which were the active curative substances in the improved diet. Recovery followed the addition of either cod-liver oil, butter, margarine containing 80 per cent. of animal fat, or olive oil. Cod-liver oil was the most effective and olive oil the least; severe cases did not improve unless cod-liver oil were given. No special virtue was found in oils containing phosphorus, other than the value of the oil in which the phosphorus was dissolved. The curative value of fats was thus found to depend on their content of A-factor.

The simultaneous increase in Central Europe of rickets in infants, late rickets in older children and osteomalacia in adults, suggested that these three diseases had a common cause; they were all cured by the administration of cod-liver oil. Looser, from pathological, anatomical and histological evidence, considers that late rickets is

a condition intermediate between infantile rickets and osteomalacia. Adults are less prone to bone disease than the growing child, but once the bone changes have appeared in the adult they are much more difficult to heal. In addition to the bone symptoms, tetany has been observed in all three diseases.

Osteomalacia before the War was usually observed in pregnant women, or in women after a succession of pregnancies. No increase of osteomalacia amongst child-bearing women was described in Vienna, and no clear connection has been traced between the osteomalacia of pregnancy and hunger-osteomalacia.

CHAPTER IX

PELLAGRA

THIS peculiar disease is endemic in the maize-eating districts of Northern Italy, Roumania, Egypt and the southern part of the United States, and is now grouped amongst diseases due to a qualitative deficiency in the diet. Pellagra usually runs a chronic course extending over many years. The disease is most active at certain seasons, generally in the spring, but the actual time varies in different regions; at the particular season a fresh outbreak occurs each year after a quiescent period. Pellagra has appeared in all parts of the world, irrespective of race or climate. People of all ages suffer from the disease; it has been recorded in an infant of 5½ months, in an old man of 99 and in a woman of 102. Women suffer far more frequently than men.

The onset of the disease is often so gradual as to be imperceptible, and the symptoms do not appear in any definite sequence. The disease in its fully developed state makes such a typical picture, that when once seen it can never be mistaken for anything else, but these cases form only a very small proportion of the whole, and the recognition of less definite cases is not simple. The pellagrin may succumb to some intercurrent infection. In uncomplicated cases there is no fever. As the disease makes its slow progress towards a fatal ending, flesh, strength and intellect fade away until the pellagrin becomes as withered as a mummy, with bones protruding through the yellow and blackened skin; death finally occurs from complete exhaustion. In mild cases pellagra is confined to slight skin and digestive troubles, and many

such cases pass unrecognised. Sometimes these mild cases recover without treatment.

Symptoms.

The most characteristic features fall into three main groups :

(1) *Severe disturbance of the whole digestive tract.*—Obstinate constipation is sometimes the first symptom, but later there is always diarrhœa. The tongue is sore and inflamed and the entire digestive tract is disordered. The hydrochloric acid secretion of the stomach is diminished, and the powers of digestion and absorption generally are impaired. The stools are liquid and exceedingly offensive and may contain mucous and blood.

(2) *Skin eruption.*—The rash is as a rule bi-laterally symmetrical, *i. e.* appears in corresponding positions on both sides of the body, on areas exposed to sunlight or to friction or pressure. The redness may be so slight as to escape notice or to be mistaken for sunburn or chaps. In a well-marked eruption the skin appears shiny, red and tense; there is a sharply defined line between the healthy and inflamed skin, which feels burning and irritable. The rash is commonly seen on the back of the hands, on the neck and in a curious butterfly shape radiating from the bridge of the nose, round the eyes and over the cheeks. The severity of the skin lesions and the stage at which they are first seen varies greatly. In communities in which pellagra is endemic, the rash appears at the same season each year, generally in spring, and after a few weeks dies away; the skin peels, leaving the underlying area pigmented a light chocolate colour. After repeated attacks the skin becomes permanently dry, shrivelled, pigmented almost black and fissured by deep cracks. The name pellagra was derived from Italian words meaning *rough skin.*

(3) *Nervous and mental symptoms.*—The onset of the disease is marked by great mental depression, headache and sleeplessness, with much disinclination for mental or physical effort. There may be vague pains in the spine and joints, and attacks of cramp, giddiness, or faintness. With each seasonal recurrence the nervous symptoms increase; depression deepens to acute melancholia or delusions of persecution; many pellagrins become suicidal or maniacal. On the other hand, many cases are sane and always remain so, but most admit to a feeling of depression and impending disaster.

There is no certain evidence that pellagra existed in Europe before Columbus introduced maize from America. The first accurate description was written in Spanish by Pedro Casal in 1707; he called it *Mal de la rosa* and described it as a new disease. From Spain pellagra spread to France, Lombardy and eastwards, wherever maize became extensively used for food by a poor agricultural population. At the present time the disease is no longer endemic in France and has greatly decreased in Spain. In Italy in 1881 there were over 104,000 pellagrins, nearly all in the northern provinces; in 1905, 53,000 cases were recorded. In Roumania the disease has increased continually since its first appearance about 1836; in 1912 it was estimated that there were about 75,000 pellagrins out of a population of 5,000,000, but the number has largely increased since the War. In the United States the disease was not recognised as pellagra till 1908. Since then the disease has appeared to increase by leaps and bounds, but some of this increase is fictitious; a better knowledge of the symptoms brought to light many cases previously unidentified. Many cases were also recalled which had escaped diagnosis in the past. During the American Civil War (1861–65) there was heavy mortality at Libby Prison, Richmond, Virginia. Maize was the principal and sometimes the only food. The prisoners developed a kind of eczema, their skin was rough and hard, their hands sore and cracked, their bowels chronically loose, and they suffered from melancholia and dementia. The whole picture is suggestive of pellagra, which was presumably responsible for the large number of deaths.

There are no complete statistics of the prevalence of pellagra in the United States. Notification is not compulsory in every State and many cases are concealed, for it is considered a loathsome disease, and the motive for concealment is strengthened by the fact that many hotels, hospitals and sanatoria exclude pellagrins. Such figures as are available show that the pellagra problem

in the Southern States is very serious. In 1916 in Carolina this disease ranked second highest amongst the causes of death; there were over 100,000 cases and about 4000 deaths in all the Southern States; during 1917 the number of cases increased by about 25 per cent. After 1917 the incidence of the disease began to decline as a result of the measures taken to check it. In the Northern States pellagra is much more rare; in both north and south Jews are practically exempt.

An epidemic of pellagra broke out early in 1916 near Port Said at the American Camp for Armenian refugees. Later in the same year pellagra began amongst the Turkish prisoners of war in Egypt, and the disease continued till the last prisoners were repatriated in 1920. Altogether there were over 9000 cases amongst 105,000 prisoners. The German prisoners of war in Egypt suffered slightly from pellagra: 79 cases amongst 7608 prisoners.

Cases of pellagra may crop up anywhere, and from time to time have been recorded in the British Isles. It is probable that many isolated cases are not identified as pellagra.

The cause of the disease baffled many investigators. It seemed impossible to track down every case to a similar origin. The association of maize and pellagra was difficult to explain; for, although it is most prevalent in maize-eating districts, yet in other parts of the world, *e. g.* Mexico, maize is eaten largely but pellagra has not been recognised; again, pellagra has often occurred in individuals who have not eaten maize. Funk (1913) was the first to observe the parallelism of maize and pellagra to rice and beri-beri. He pursued the analogy too closely in assuming that pellagra was caused by the loss of some food-substance in the milling process of maize, and failed to substantiate his theory.

Casal, in his original description of the disease, had associated it with a poor diet, and remarked that " the patients obtained great relief when their food (which contained no meat) was replaced by other substances of

a more sustaining kind." Goethe in his *Italian Journeys* (1816) mentioned the pitiful condition of the Tyrolese peasants, and thought it was caused by their food, which was corn, fruit, green haricots and sometimes a little cheese, " they ate no meat the entire year; " the symptoms he described correspond with those of pellagra. Townsend in his *Travels through Spain* (1789) gave the first description in English of this disease, and said that it originated amongst people " who ate little flesh in their food." Their diet was Indian corn (= maize), beans, peas, chestnuts, apples, pears, melons and cucumbers.

Towards the close of the nineteenth century the association of pellagra with a diet poor in meat was lost sight of, owing to the growth of the new science of bacteriology and the tendency to ascribe every disease of unknown cause to some positive agent, such as a micro-organism or a toxin produced by a micro-organism. Pellagra at one time was supposed to be due to a toxin formed in maize by the action of moulds or bacteria, and at other times to be a direct infection. The belief in its infectious nature was predominant at the time of the discovery of pellagra in the United States. Various commissions were formed to study the disease with the primary object of determining whether it was caused by an infection or by an error in the diet.

Dr. Joseph Goldberger and his colleagues, who began their investigations in 1914, found that it was not possible to reproduce the disease either in man or animals by feeding or inoculating with secretions or with any sort of material likely to contain infection from cases of pellagra. Goldberger drew attention to observations made in European institutions for the segregation of pellagrins, that the disease did not spread from the patients to the staff in spite of the absence of any special precautions. He discovered the same freedom from pellagra amongst the nurses and attendants in various orphanages and lunatic asylums in the United States in which there were outbreaks of pellagra.

Two instances recorded by Willets were quoted by Goldberger:

In Georgia State Sanitarium, 7·65 per cent. of the patients remaining over one year developed pellagra; there were no cases among 293 attendants who had been in intimate contact with them all the time.

In the Orphanage at Jackson, Missouri, 68 out of 211 children (32 per cent.) developed pellagra. Two cases were amongst children under six; one case amongst children over twelve; all the other cases were amongst children aged six to twelve years. The housing and general conditions of life were the same for children of all ages.

The exemption of the older and younger groups of children was as inexplicable on the basis of infection as the exemption of the attendants in Georgia State Sanitarium. The only constant difference which could be detected was in the diet. At both institutions those free from pellagra had a better diet containing more meat, milk, eggs, etc.; those who contracted the disease had little fresh animal food and a great deal of maize and syrup.

In some other institutions there was an obvious difference between the diet of the staff and of the patients, whilst in those in which no difference was supposed to exist, a minute examination showed that although the food was theoretically the same, yet actually there was a difference. The nurses availed themselves of their privilege of selecting the best and most varied food from the institutional dietary, and also supplemented it from outside.

The prevalence of pellagra in the cotton-mill districts of South Carolina was also found to be related to the diet. In the pellagrous households the food, though satisfying the standards of energy value and of quantity of protein, which was derived mainly from cereals, beans and peas, contained too little protein of animal origin. In the non-pellagrous households more eggs, meat, milk and cheese were used. The pellagrous households generally used

rather less carbohydrate food, thus excluding any connection between pellagra and an excessive amount of carbohydrate. The prevalence of pellagra in this district was directly associated with the poor supply of meat and milk: there were no dairies or butchers' shops; little meat or poultry was produced locally, and few cows were kept.

Additional evidence of the association of pellagra with an unbalanced diet came from many sources. The distribution of pellagra in Catto Parish, U.S.A., quoted by Dr. A. A. Herold, is a good illustration. Here agricultural and mining districts lie side by side; the general hygienic conditions favour the agricultural community, who are the sufferers from pellagra.

Mineral Oil District.	*Agricultural District.*
Bad sanitation, flies, mosquitoes.	Better sanitation, fewer flies, etc.
Typhoid and malaria frequent.	Typhoid and malaria less frequent.
Diet, thoroughly mixed and varied.	Diet, chiefly fat pork, corn-meal and syrup.
No pellagra.	200 cases of pellagra.

Goldberger concluded that pellagra was in no sense of the word a communicable disease, but connected with the food. The chief foods of pellagrous districts and institutions were vegetables and cereals. He therefore suggested that the disease might be prevented by reducing the quantity of cereals and increasing the amount of fresh animal foods such as meat, milk and eggs. This recommendation was put into practice at two orphanages in Jackson, Missouri, and pellagra was eliminated.

The cereal diet of the pellagrins is generally necessitated by poverty and the high price of meat, milk, fish and eggs. In the winter the diet is limited to the cheaper vegetables, cereals, carbohydrates and fats, such as sweet-potatoes, maize, syrup and "sow-belly" fat. A rise in the price of food, especially of meat, poultry and eggs, as Sydenstricker (1915) showed, was followed by an increase of pellagra. A fall in wages at the same time had necessitated sacrifices in the variety, quality and quantity.

In the poorer asylums the prevalence of pellagra was due to fewer and less skilled attendants, who were unable to care for the patients individually and to see that each actually consumed his share of the food. There were more cases of pellagra amongst the so-called " untidy " group of patients who could not feed themselves properly, and who allowed their plates to be robbed by other patients known as " stealers." In all parts of the world it is the " untidy " class of asylum patients who suffer from pellagra, scurvy, or beri-beri.

Goldberg therefore added to his earlier recommendation the caution that it is necessary to see that the good food provided is actually eaten by each individual. The need for this caution was endorsed by Colonel Vaughan, who had difficulty in making the men of the Southern Army camps eat the good ration provided. They had been accustomed at home to eating corn-bread, fat pork and corn syrup, and if they could get these would eat nothing else.

In general, it was concluded that pellagra does not develop amongst those who eat a varied and well-balanced diet. No cases have been described either on the rations issued to the United States Army and Marine Corps or to the Italian troops, though both in Italy and the States many of the recruits come from pellagrous districts.

Goldberger, assisted by Wheeler, verified all his conclusions by an actual experiment. With the bribe of a free pardon from the Governor of Mississippi, eleven healthy convicts, who had never suffered from pellagra, were induced to volunteer for a feeding experiment to ascertain if the disease could be produced in healthy white men by a one-sided, chiefly cereal diet. The experiment was carried out at Rankin Farm belonging to the State Penitentiary, where there was no previous history of pellagra. The hygienic conditions were excellent and special precautions were taken to exclude flies and any infection which they might carry. To reduce further the possibility of infection, the " pellagra squad," as they

were called, were segregated and kept under observation for a preliminary period on the ordinary prison diet. They were then given a diet of biscuits, white wheat flour, various maize preparations, gravy, syrup, sugar, coffee, collards, cabbage, sweet-potatoes, turnips and turnip greens, rice and fat pork. The daily quantity per man had an energy value of about 3000 Calories per day, sufficient considering the very light work done. As controls, thirty-five other prisoners, four free women and two children, were kept on an ordinary mixed diet containing some meat, eggs and buttermilk. They lived under inferior hygienic conditions and no precautions were taken to protect them from any infection. During the second month of the experimental diet all the pellagra squad complained of weakness, headache, abdominal pain or some other discomfort. After five months skin eruptions were noticed in six men; the symptoms were pronounced by experts to be those associated with pellagra. The experiment had to be discontinued at this stage, owing to the refusal of the prisoners to continue. During the last four weeks all the prisoners on the experimental diet had shown marked loss of body weight and all were out of health. Pellagra thus developed in six out of eleven men, and would probably have developed in all if the diet had been continued a little longer. Indeed Wilson, from his experiences with the outbreaks in Egypt during the War, considers that four other cases might well have been included as pellagrous from the peculiar intestinal and lingual symptoms described. There was not a single case of pellagra amongst the controls; they remained in good health.

Goldberger's work has been approved by Colonel Vaughan and Dr. Welch, who were appointed by the Public Health Service to examine it. His results are in accordance with the original observations of Casal, Townsend and Goethe, that meat was seldom eaten in pellagrous districts, and exclude the possibility of infection as the cause of the disease. Variation in the

composition of the diet accounts for the seasonal epidemics of the disease. Lombroso's data show the seasonal change in the diet in Italy:

	Eight Winter Months.	Four Summer Months.
Polenta (maize)	1,000 grms.	160 grms. per day.
Bread (partly maize)	100 ,,	600 ,, ,, ,,
Meat	10 ,,	60 ,, ,, ,,
Cheese	5 ,,	20 ,, ,, ,,
Beans	150 ,,	40 ,, ,, ,,
Milk and eggs	0 ,,	0 ,, ,, ,,

Smaller quantities of meat and cheese are used in the winter and more maize and beans.

The value of animal protein in preventing pellagra was again exemplified by the distribution of pellagra during the War. All the troops with their high meat ration were free from this disease, though they suffered at times from beri-beri or scurvy. In Roumania the civilian population, whose chief food was maize, were terribly afflicted with pellagra, but the Roumanian Army, which was well supplied with meat, escaped the disease. The epidemics of pellagra in the refugee and prisoners' camps in Egypt were connected with the small ration of animal protein.

A diet containing meat, milk, fish and eggs will cure cases of pellagra which have not progressed too far; a return to the former poor diet naturally will cause a relapse. Advanced cases are very difficult to cure, as the digestion may be so disordered that protein cannot be assimilated. Digestion is greatly helped by the administration of hydrochloric acid (physiological strength = 0·2 per cent.) in addition to good food. The diarrhœa which is so common in pellagra has been found to be a sign that the gastric secretion is deficient in hydrochloric acid.

Goldberger and his associates in America, and Wilson and other workers in Egypt, have proved beyond question that pellagra follows if the food for a long period has been poor in animal protein, although the total amount of protein in the diet satisfies the physiological standard and there is no shortage of vitamins. The quality of the protein is the determining factor.

CHAPTER X

THE QUALITY OF PROTEIN AND PELLAGRA

THE protein constituent of the food differs from all the others by its endless variety. Egg-white and meat protein are quite distinct proteins. Milk contains two kinds of protein: the casein which is used to make cheese, and an albumin, like egg-albumin, in the whey. The presence of protein in cereals is obscured by starch, yet about one-tenth of wheat flour is protein; in fact, two very special proteins are present: gliadin, soluble in alcohol; and glutenin, insoluble in alcohol but soluble in dilute alkali.

The proteins are classified by their physical differences, such as their solubility in different solvents, heat coagulation, etc. It is not as yet possible to classify them according to their chemical analysis, which is very difficult and is still incomplete.

The work of Fischer, Kossel and their pupils has shown that proteins on hydrolysis, *i. e.* by boiling with strong mineral acids, break down into about twenty different amino acids. These units can be arranged in eight groups according to their chemical nature:

(1) *Simple Mono-amino Acids.*
Glycine, alanine, valine, leucine and iso-leucine.

(2) *Mono-amino-dibasic Acids.*
Aspartic acid and glutamic acid.

(3) *Hydroxy-amino Acids.*
Serine and hydroxyglutamic acid.

(4) *Heterocyclic Acids.*
Proline and hydroxyproline.

(5) *Mono-amino Acids with Aromatic Nucleus.*
Phenylalanine and tyrosine.

(6) *Mono-amino Acid with Indole Nucleus.*
Tryptophan.

(7) *Hexone Bases or Diamino Acids.*
Lysine, arginine and histidine.

(8) *Thio-amino Acid.*
Cystine.

The chemical analysis of the protein shows that the various proteins yield different amounts of the amino acids. Some of the data are shown in the following table; the peculiarities of each protein are indicated by the figures in heavy type:

	Ox Muscle.	Casein.	Lact-albumin.	Gelatin.	Wheat gliadin.	Wheat glutenin.	Maize zein.	Maize glutenin.	Hemp edestin.	Sturin.
Glycine	2·1	0	0	**19·3**	0	0·9	0	0·3	3·8	
Alanine	3·7	1·5	·25	3·0	2·0	4·7	9·8		3·6	
Valine	0·8	7·2	0·9		3·4	0·2	1·9		+	
Leucine	11·7	9·4	**19·4**	6·8	6·6	6·0	19·6	6·2	20·9	
Phenylalanine	3·2	3·2	2·4	1·0	2·4	2·0	6·6		3·1	
Tyrosine	2·2	4·5	0·9	**0**	1·2	4·3	3·6	3·8	2·1	
Serine		0·5		0·4	0·2	0·7	1·0		0·3	
Cystine				**0**	0·5	0·02			0·3	
Proline	5·8	6·7	4·0	10·4	**13·2**	4·2	9·0	5·0	4·1	
Hydroxyproline		0·3		6·4					2·0	
Aspartic Acid	4·5	1·4	1·0	1·2	0·6	0·9	1·7	0·7	4·5	
Glutamic Acid	15·5	15·6	10·1	1·8	**43·7**	**23·4**	**26·2**	12·7	18·7	
Tryptophan	+	1·5		**0**	1·0	+	**0**	+	+	
Arginine	7·5	3·8	3·2	9·3	3·2	4·7	1·6	7·1	**14·4**	**58·2**
Lysine	7·6	6·0	**9·2**	5·0	0·2	1·9	0	3·0	1·7	**12·0**
Histidine	1·8	2·5	2·1	0·4	0·6	1·8	0·8	3·0	2·4	12·9

In general, the albumin group of proteins contains all the amino acids, except glycine, in various proportions. The globulin group is similar, but contains glycine, and has, in addition, a higher amount of glutamic acid, especially those globulins of vegetable origin. The phosphoproteins (casein) resemble the albumins, with no striking preponderance of any single amino acid. The gliadin group of cereal proteins is peculiar in its high content of glutamic acid and proline. Sturin, the protein of fish sperm, is made up of the three hexone bases

with no, or very little, mono-amino acids. Gelatin lacks cystine, tyrosine and tryptophan. These are merely some of the most obvious differences. Proteins thus differ markedly in quality.

Our analytical data are far from complete; in no case do the totals of the amino acids add up to 100. The incompleteness is chiefly due to the great difficulty of separating and estimating the individual amino acids. There may be still some unknown amino acids in small quantities; *e. g.* hydroxyglutamic acid has been discovered recently by Dakin by a new extraction method. This method may lead to further discoveries; once again it has proved that every new process in connection with the chemistry of the proteins has given a valuable result.

The work of Fischer and Kossel has also revolutionised our conception of protein metabolism. We no longer think, like Liebig and others, that the protein of the food becomes directly the protein of the body, for it has been demonstrated by physiologists that the protein of the food is split up during digestion into its constituent amino acids, that the amino acids circulate in the blood, and that the tissues select the amino acids from which their protein is built up. All proteins are digestible by man except the scleroproteins, such as horn, hair, silk, etc., which are therefore useless as food.

Differences in proteins may be due not only to a variation in the relative amounts of the amino acids which they contain, but also to differences in the manner in which they are arranged. The protein molecule may be pictured as a continuous chain of amino acids coiled upon itself. This method of combination allows theoretically of endless variation; if only three amino acids are taken they can be arranged in six different ways:

a–b–c, b–a–c, c–b–a, a–c–b, b–c–a, c–a–b.

With eighteen or twenty amino acids the number of arrangements is almost infinite. Two proteins may contain exactly similar amounts of amino acids and yet be

distinct because of a difference in the sequence in which the amino acids are connected. On this basis the difference which exists between the blood and milk proteins of various species of mammals may perhaps be explained.

All the amino acids are required by the animal body for building up its various tissues, but with the exception of glycine, the simplest unit, and possibly of proline, the amino acids cannot be formed in the animal organism, which is therefore ultimately dependent upon the vegetable world for its protein supply. Our animal food is derived from the grass eaten by cattle. The plant proteins during digestion are split up into the various amino acids and built up into proteins of quite different pattern; that is, containing amino acids in different proportions and sequence. During this reconstructive process there may be great waste of some amino acids. For example, if the protein of ox-muscle, which contains about 16 per cent. of glutamic acid, has to be built up from food in which the only protein is wheat gliadin, containing over 40 per cent. of glutamic acid, there is a large waste of glutamic acid. Further, the muscle protein requires about 8 per cent. of lysine for its construction, but gliadin contains only 0·2 per cent. of lysine. In order to obtain sufficient lysine, 40 parts of gliadin are required to construct one part of muscle protein, so that the waste of glutamic acid is again increased. Cannibalism is thus the most economical method of nutrition, as for each part of muscle protein in the food it is theoretically possible to build up one part of muscle protein in the body. The nearest parallel that there is to cannibalism is the nursing of the infant by its mother. In general, for the building of muscle protein, the flesh of animals is the best food.

Proteins can thus be classed as good, poor or incomplete for nutritional purposes. The good proteins are those which are converted with little waste of amino acids into the body proteins. The poor proteins contain all the amino acids, but in unsuitable proportions involving much waste of certain amino acids. The incomplete proteins, such as

gelatin and zein, do not contain all the essential amino acids (see table, p. 101).

The proteins of seeds, including cereal grains, are generally speaking poor proteins, as they contain unsuitable proportions of the amino acids. The proteins of green leaves, owing to difficulties in the way of chemical manipulation, have not yet been analysed. Herbivorous animals live naturally on a diet in which the protein is derived practically entirely from green leaves with a small proportion of seeds. There is a record, though this can scarcely be considered scientific evidence, that Roman soldiers sometimes lived on a diet of peas and cresses, that is, of leaf and seed. The digestive systems of man, pigs and carnivores are not adapted for dealing with a bulk of material containing cellulose, such as the herbivores eat. So-called vegetarians usually indulge in some animal protein, *e. g.* milk, cheese, or eggs, but a truly vegetarian diet may suffice if it is rightly selected as to its amino-acid content and is not too bulky. Mixtures of seed, nut and leaf proteins may contain all the essential amino acids in sufficient amount. It is the excessive preponderance of proteins derived from cereals or seeds alone which constitute a dangerous diet likely to produce pellagra.

The function of any individual amino acid may not be limited to its share in building up tissue protein, it may play some part in the vital processes; *e. g.* the iodine of the thyroid is present as an indole compound, and the amino-acid tryptophan, an indole derivative, may be indispensable for the maintenance of the thyroid function. In the same way tyrosine or phenylalanine seem to be necessary for the formation of adrenaline by the suprarenal glands.

The biological effect of the individual amino acids can only be tested by feeding experiments. The practical difficulties of feeding animals with a mixture of pure amino acids are far too great, because of the labour involved in their preparation. The plan adopted is to feed

the proteins which are known to be lacking in certain amino acids and compare the result with the feeding of the same food plus the missing unit or units.

The first experiment of this kind was made by Hopkins and Wilcock in 1906. They selected zein (from maize) as protein, which was amplified with the addition of 2 per cent. of its amount of tryptophan. Young mice on the zein alone immediately began to lose weight and generally died in 16 days; decline in weight also occurred in another set with added tryptophan, but death did not occur until the 30th day. Adult mice lived 27 days without tryptophan, and 49 days with tryptophan. Tryptophan had thus an appreciable effect on the survival period of the animals, but as zein is incomplete in respect of other units, the addition of tryptophan alone was not sufficient to maintain normal life.

The experiment was repeated by Ackroyd and Hopkins under better conditions. The amino-acid supply was derived from casein in which the tryptophan had been destroyed by acid hydrolysis, but the mixture contained all the other units. Tryptophan was at first added to the mixture, but omitted after the twelfth day and included once more on the thirty-fifth day. There was growth during the first period, decline in weight during the second period, followed by growth on inclusion once more of the tryptophan. This is shown by the continuous lines in Fig. 20. The upper dotted line shows continuous growth on the complete mixture; the lower dotted line shows loss of weight in the absence of tryptophan.

Similar experiments made by Osborne and Mendel in America on young rats showed that zein produced growth if supplemented by tryptophan and lysine, but even then the growth was not entirely satisfactory. These workers also tested on growing rats the effect of wheat gliadin as sole source of protein; it contains all the amino acids, but some of them, particularly lysine, are only present in very small proportions. Adult rats were maintained for quite long periods, as long as 500 days,

but young rats fed on gliadin lived but did not grow. The growth impulse was not destroyed but remained dormant; if the diet was changed to natural food at an

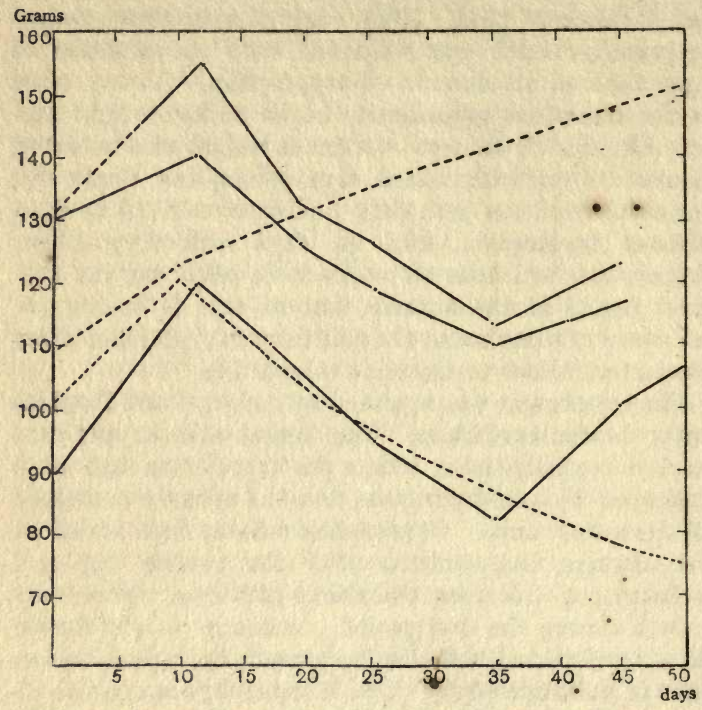

FIG. 20.—Weight charts of rats showing the effect of withdrawing tryptophan from the diet (Ackroyd and Hopkins). Ascending dotted line shows the average growth of 16 rats on complete amino acid mixture. Lower and descending dotted line shows the average loss of 8 rats on diet without trytophan. Continuous lines show average weight of 2 rats in each case. Tryptophan was removed on 12th day and restored on 35th day.

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age at which growth had normally ceased, the improved diet caused the resumption of growth until full adult size was reached.

In later experiments lysine was added at intervals and growth took place during the periods in which lysine

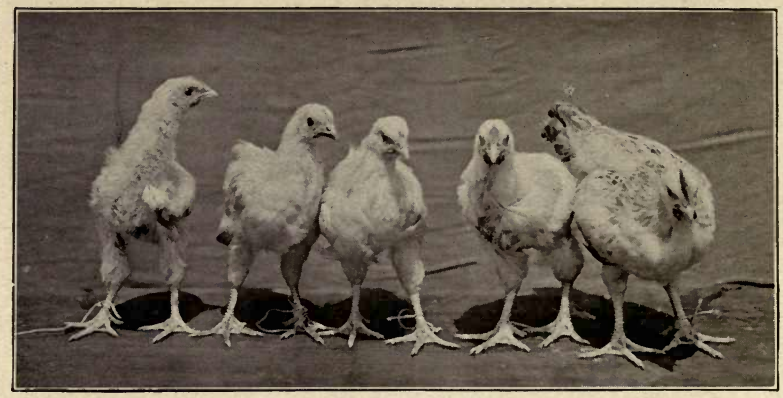

FIG. 22.—Chickens on grain mixture of high lysine content.

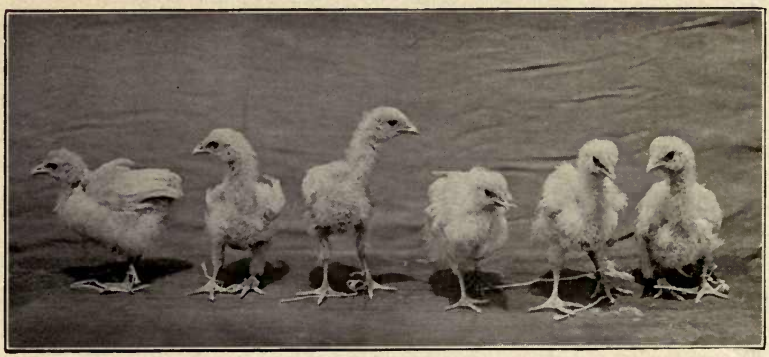

FIG. 23.—Chickens on grain mixture of low lysine content. Chickens in both figures of same age (Buckner, Nollau and Kastle).

Reproduced by kind permission from Bulletin No. 197, Kentucky Agricultural Experimental Station, 1916.

was given, but not in the periods without it; the effect is clearly shown by the weight charts, Fig. 21.

The effect of lysine upon growth has also been demonstrated by Buckner, Nollau and Kastle in the case of chickens living under the natural conditions of a poultry farm. Birds were fed upon grain mixtures of high or low lysine content, and, as their photographs show (Figs. 22 and 23), more rapid growth took place on the mixture of high lysine content.

Those proteins which are naturally concerned with the

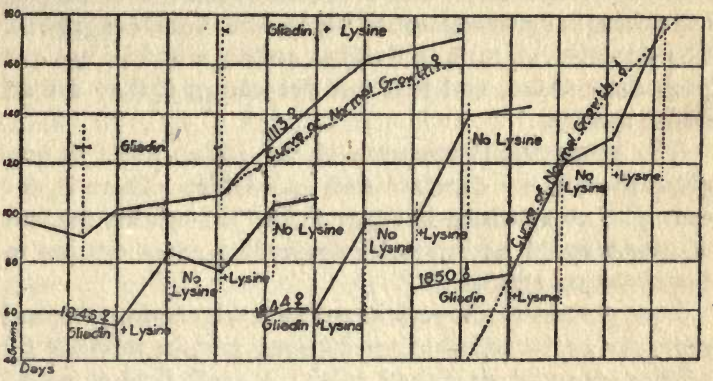

FIG. 21.—Weight charts of rats showing indispensability of lysine for growth (Osborne and Mendel).

Reproduced by kind permission from *Journal of Biological Chemistry* (Baltimore), 1914, 17, 342.

growth of young animals, such as casein and lactalbumin in milk and vitellin in eggs, all show a relatively high content of lysine, while it is entirely absent from some vegetable proteins, such as hordein from barley and zein from maize.

No amount of energy value, nor of protein, in the food, however abundant, can induce growth in young rats unless lysine be present. It is thus useless to emphasise, as Rubner and others have done, the quantitative aspect of the protein requirement for growth unless the quality of the protein is kept clearly in mind.

The element sulphur is present in proteins in the amino-

acid cystine, though it is possible that other sulphur-containing units may be present. If a protein contains very little cystine, it will not produce normal growth. Phaseolin, the chief protein of the haricot bean, is deficient in cystine; kafirin, a protein from millet, is deficient in cystine and lysine; casein is also poor in cystine.

In addition to tryptophan, lysine and cystine, the amino acids, tyrosine and phenylalanine, containing aromatic nuclei are probably also essential. The di-amino acids, histidine and arginine, appear to be inter-related in nutrition; absence of both causes loss of weight, but absence of either alone merely lessens the rate of growth. The function of each individual amino acid has not yet been determined, and it is not yet known if they are all indispensable.

The proportional amounts of the amino acids in any given protein are constant and invariable. There is, for example, no evidence to suggest that the cystine content of casein could be increased by feeding extra cystine to the lactating animal.

Poor protein foods, such as maize meal, can for practical purposes be turned into an efficient protein mixture by adding an equal weight of milk. A great deal of useful work is being done to determine which are good proteins and to find the most practical method of supplementing poor ones. The proteins of cereals, on account of their extensive use as food for man and beast, have been the centre of interest. At first sight it seems strange, if pellagra be produced by a diet low in animal protein and rich in cereal, that there should be no pellagra associated with a beri-beri producing diet of white polished rice with little meat, the staple diet of so many millions in the East. An investigation of the chemical nature of rice protein has shown that it more closely resembles an animal protein in its amino acid make-up than does any other cereal protein. In this connection words spoken by Hopkins as long ago as 1907 have acquired an almost prophetic value: "This matter of qualitative differences of proteins

may be of no small significance in dietaries. It may account for what I believe is proved by experience—that rice may serve the races which rely on it as an almost exclusive source of protein, while wheat is only suitable for races which take a much more varied dietary."

Rice contains better protein than wheat, and wheat better than maize. The relation of maize to pellagra, which for so long was inexplicable, now becomes clear. Pellagra follows the deprivation of certain amino acids which are not supplied in sufficient amount by maize. It does not develop if, in addition to maize, there is present in the food some protein which suitably supplements the deficiencies of the maize. Pellagra develops upon a diet containing insufficient good protein even if no maize be eaten. Pellagra may develop in spite of good protein in the food if any diseased condition of the digestive tract prevents the digestion and assimilation of protein, *e. g.* after dysentery or after certain operations.

It is not yet determined which of the amino acids are essential for the prevention of pellagra, but as tryptophan, lysine, cystine and other amino acids are indispensable for the formation of tissues, it is possible that the deficiency of any one of them is a factor in the development of the disease. The varying forms in which pellagra manifests itself may be accounted for by the supposition that in one case the deficiency of tryptophan may be the greatest, while in other cases cystine or lysine, etc., may be more deficient than tryptophan, the diet of no two pellagrins being exactly similar in their amino-acid content.

Chick and Hume (1920) carried out experiments on three monkeys to determine the effect on them of prolonged feeding with a diet of poor protein. The three vitamins were given in ample amount and the energy value of the food was sufficient. About 70 per cent. of the total protein consisted of zein, *i. e.* of maize protein; the diet was therefore known to be deficient in tryptophan and lysine. After periods of 49, 51 and 117 days respectively, all three monkeys

developed bi-laterally symmetrical skin eruptions resembling pellagra in man. The animals lost weight slowly, became weak and ill, but only one had diarrhœa, and none showed the nervous symptoms associated with pellagra. The addition of tryptophan to the food, if given in time, improved the general condition, but weight was not regained. The further addition of a mixture of lysine, histidine and arginine had no marked effect. The daily addition of 5 to 10 grams of plasmon (= casein) caused the skin lesions to disappear, but lost weight was not regained until a normal diet of rice, wheat germ, milk and cabbage was given. The experiment is of significance as it offers additional evidence that a condition resembling pellagra is produced by a diet containing protein poor in quality.

Besides the feeding of diets varying in amino-acid content there is another practical method of determining the biological value of a protein. In this method the amino-acid composition is not considered, but its efficiency is estimated by determining the least quantity of a given protein which is required daily to keep an average man of 70 kilos. from loss of body weight; that is, in nitrogenous equilibrium. This method was first employed by Karl Thomas in 1909, and from the results he obtained by feeding experiments on himself, he was able to make a comparative table of the biological value (= B.P.V.) of the proteins in common food-stuffs. Milk protein was taken as the standard and assigned a value of 100.

Smallest Daily Amount to Protect a Man of 70 kilos. from loss of Body Weight	Grams.	B. P. V.
Beef	30	104
Milk	31	100
Fish	33	94
Rice	34	88
Potato	37	79
Pulse (pea or bean)	54	55
Wheat	76	39
Maize	102	29

The figures assigned by Thomas are only an approximation and their practical value has been questioned. Wilson, who has studied the diets associated with pellagra

in Egypt, has found a calculation of the biological value of the protein by Thomas's method to be a reliable guide. It is obvious that a diet containing a sufficient amount of protein, according to the 100 grams standard (p. 10), is physiologically inefficient if the protein is derived almost entirely from cereals such as maize.

In order to estimate approximately the B.P.V. of a mixed diet the total quantity of each protein must be divided by a factor; the factors used by Wilson were:—

For Animal protein	1·0
,, Rice	1·12
,, Potato	1·27
,, Pulse	1·82
,, Wheat	2·55
,, Maize	3·4

In planning a diet the minimum requirement should not be approximated too closely. For instance, the 30 grams of animal protein daily, which are sufficient under the favourable conditions of a laboratory experiment, are probably insufficient under the changing conditions of ordinary life. These minimal protein quantities only suffice if the rest of the diet is of proper Calorie value. Individual variations must also be borne in mind when planning a dietary for a large number of people; a diet sufficient in protein for the majority might be deficient for some individuals. Wilson advises that the protein should have a biological value equal to at least 40 grams of animal protein.

On these principles Wilson has proved that the outbreaks of pellagra in refugee and prisoners' camps in Egypt were due to a poor protein diet. The diet of Turkish prisoners of war doing no labour had a B.P.V. of 38·6; those on moderate labour 48·2. There were more cases of pellagra amongst the labour group in spite of their diet of better B.P.V.; the effect of work upon the protein requirements is thus indicated. The same effect of

muscular work was observed amongst Egyptian civilian prisoners. Convicts at hard labour with a diet higher in B.P.V. than that of convicts on moderate or no labour yet suffered more frequently from pellagra. Labour is thus a factor in the causation of pellagra in a community where the good protein supply is on the border of insufficiency. Defective absorption, brought about by faulty methods of preparation, may also be a determining factor on a border-line diet.

The diets which produce and cure pellagra have been examined by Wilson and their B.P.V. determined. These values have been put together in a table, and summarise his work upon the subject.

PELLAGROUS DIETS.

	Available Protein.	B. P. V.	Animal Protein.	Calories.
Armenian Refugee Camp, Port Said, May 1916	grams. 51·5	grams. 23·0	grams. 4·0	daily. 2160
Goldberger's Rankin Farm Experimental Diet	35·0	14·6	0·4	2836
Italian peasant, light labour	60·1	30·4	8·0	2020
Turkish prisoners of war, Egypt, 1918: non-labour	60·0	33·5	10·0	2825
hard-labour	63·0	36·8	13·7	2903
Egyptian convicts: light labour	69·5	33·5	6·0	3062
hard labour	82·7	48·3	22·8	3195
Abassia Asylum	78·0	46·4	22·0	2910
Egyptian native boy aged 11	29·0	10·4	0	1667
DIETS WHICH CURED PELLAGRA.[1]				
Armenian refugees	83·0	59·1	39·5	3143
Egyptian convicts, resting	82·7	54·7	29·4	2871
Egyptian native boy, aged 11, not resting	43·5	24·9	14·5	
NON-PELLAGROUS DIETS.				
Japanese prisoners, 1911	39·0	37	0 (99 per cent. rice)	2110
English sewing-girl	62·0	45	21·5	2563
Scottish convicts, hard labour	105·0	66	54·6	3709
Better-class English diet	91·6	80	45	2681

[1] Very advanced cases not cured.

The modern work on the quality of protein gives the explanation of the insufficiency of gelatin as a food, discovered during the French Revolution, and suggests that pellagra may have existed in English gaols early in the nineteenth century among prisoners on a bread-and-water diet. During the French Revolution food was scarce and gelatin was extracted from bones and made into soup for the use of the poor and for hospitals. The soup was made palatable with salt, vegetables and sometimes a little meat. Increased mortality followed its use and a commission was appointed to discover the reason. Some members of the commission tried the soup and found its continued use caused indigestion, nausea, burning thirst and diarrhœa. It was concluded that the soup contained insufficient nutriment and was detrimental to health. The physiologist Magendie was appointed to make further investigations. He fed dogs with gelatin; they ate it greedily at first, but it caused profuse diarrhœa. Dogs kept together soon left the gelatin untouched and ate each other; if kept separately they refused the gelatin but drank water. Variations in the flavouring made no difference. One dog, kept on bread and gelatin for 63 days, had profuse diarrhœa all the time, but was cured in four days by changing the diet to meat. Magendie considered that the diarrhœa was directly due to the gelatin and not from the want of some elementary principle in the diet. Budd (1842) disagreed with Magendie's verdict and attributed the symptoms to something wanting in the diet, for he had been greatly impressed by the frequency with which diarrhœa followed upon a bread-and-water diet in our prisons, and he mentioned especially the experiences at Millbank Penitentiary. There, in July 1822, the ration was changed and the animal part of the diet reduced almost to nothing. In the autumn the prisoners visibly declined—" those at the mill could grind less corn, those at the pump could raise less water." In the following spring, in addition to much scurvy, 48 prisoners came into hospital with diarrhœa of a peculiar

kind, impaired digestion, diminished strength, various nervous symptoms and mental despondency (cf. early symptoms of pellagra, p. 91). Between 800 and 900 patients were affected in this way; those longest in prison suffered most, *except* the officers and staff and those prisoners who assisted in the kitchens, all these escaped the illness. This exemption of certain groups in the same surroundings, but with better food, suggests that the disease was the result of a food deficiency and not of a contagious nature.

From these and similar experiences it became common knowledge that animal food-stuffs had some special value in nutrition, and that gelatin, although a nitrogenous animal product, was not a substitute for meat.

CHAPTER XI

THE EFFECT OF PARTIAL DEFICIENCIES IN THE FOOD

THE earliest signs of malnutrition from poor quality protein or from lack of vitamins are so indefinite that their significance is not realised. Unmistakable symptoms do not appear until the damage has made considerable inroads upon the health. Beri-beri symptoms are not obvious before 60 days; scurvy not before 4 months; pellagra not before 5½ months; and if there is a certain, but too small, amount of the protective substances in the diet the appearance of definite symptoms is delayed. During the whole of this time the effect of the deficiency is undermining the health. The only warnings of malnutrition are perhaps headache, lassitude, digestive disturbances, depression and loss of appetite; all these symptoms may be due to quite other causes.

Between the complete absence of any one vitamin, causing beri-beri, scurvy, etc., and a diet containing a sufficient quantity of all the vitamins, numerous variations are possible and many people exist upon a diet between these two extremes. The value of a diet cannot be judged by its palatability and apparent variety. The unpalatable and monotonous diet adopted in Denmark during the war is in striking contrast to a common diet of the poorer classes in this country, as shown on the next page.

The Danish diet contained all the vitamins, and good protein was provided by the milk; meat was practically unobtainable except by the very wealthy. During the period of its consumption the death-rate fell by 34 per cent., thus demonstrating its efficiency. From

this experience Hindhede, a Danish physiologist, concluded that "the principal cause of death lies in food and drink."

Danish War Diet.	British Working-class Diet.
Bread made of whole rye + wheat bran + 24 per cent. of barley.	Bread, cakes and puddings made from white wheat flour and other prepared cereals.
Barley porridge.	Oatmeal porridge.
Potatoes.	Potatoes.
Greens.	Meat and vegetable stew.
Milk in considerable quantities.	Margarine.
Butter.	Corned beef, tinned salmon, etc.
	Bacon.
	Kippers, bloaters, smoked haddock.
	Cheese.
	Milk in small amounts.
	Jam, pickles, sugar, syrup, tea, coffee, cocoa.
	Sago, tapioca, pea flour, etc.

The nature of the deficiency in the British working-class diet is not the complete absence of any one vitamin but a shortage of all of them; neither A-, B- nor C-factor is present in abundance and may be further reduced by methods of cooking. The diet contains few natural food-stuffs which have not been prepared or preserved in some way. The occasional addition of eggs, fruit and real butter, the daily use of potatoes and of small quantities of milk, avert rapid disaster, but the diet is not consistent with good growth in children nor with good health in persons of any age.

The Danish war diet consisted entirely of natural food-stuffs. McCarrison refers to another example of a monotonous diet which is good because it contains only natural foods. The people of the state of Hunza, in the extreme north of India, live solely on wheat, barley, maize, fruits, especially apricots, goats' milk and butter; goats' flesh is only eaten on feast days. The people are unsurpassed in perfection of physique and freedom from disease in spite of the hard climate and lack of sanitation; appendicitis is unknown; they have an extraordinarily long span of life.

Sir James Mackenzie has recently emphasised the need for research to study the early symptoms of disease, tracing its origin back to the elusive point of departure from perfect well-being. In carrying out feeding experiments upon animals, one cannot but realise that the balance between health and disease, even between life and death, is actually under control. The scales are so sensitive that they may be swayed in one direction or the other by the addition or subtraction of seemingly trifling quantities of certain food-stuffs. A growing animal, provided with plenty of food, can be stunted at will, made to decline almost to the point of death and restored with miraculous suddenness by a slight readjustment of the diet.

One of the earliest signs of inadequacy of diet is a lowering of resistance to infection. In the laboratory, control animals on a normal diet remain healthy, while neighbouring animals on a deficient diet suffer from epidemics of often fatal diseases of the lungs, eyes and digestive tract. The hygienic conditions are the same for all, but the infections do not spread from the ill-fed to the well-fed. It is not to be inferred from this that the spread of such diseases as scarlet fever, small-pox or measles can be checked by attention to diet, but there is a considerable amount of evidence which indicates that certain diseases, such as tuberculosis, pneumonia, ulceration of the cornea of the eye, dysentery and inflammatory conditions of the digestive tract, show a marked predilection for people on an unbalanced diet. Influenza may possibly belong to this category; certain individuals get it again and again, while others never take it even when often in contact with the disease. The United States Public Health Reports (1919) record the failure to infect 78 volunteers, either by cultures or secretions from virulent cases of influenza. This fact suggests that lowered resistance is a necessary factor before the infection can establish itself; in many cases the lowered resistance may result from food lacking in vitamins. In

an old manuscript [1] it is reported that an epidemic sickness (resembling influenza in its symptoms) spread in 1647 all through North America; five to six thousand died in St. Christopher's alone, and as many in Barbadoes. "This devastating sickness followed on a great drought which burned up all the potatoes and other crops." Influenza again raged round the world during the lean years of the war, and just after a general failure of the potato crop in 1916. Dr. J. Brown stated, at the British Medical Association Congress, 1920, that in his experience the allotment holders consuming their own fresh-cut vegetables resisted influenza much more easily. He attributed the general lowered resistance of the people to the increased use of preserved foods.

Feeding experiments on animals and clinical experience with human beings have proved that the cases of deficiency disease which are most intractable to treatment, and are often incurable, are those slow, chronic cases arising from a partial deficiency continued over a long period. This long-continued partial deficiency of vitamins in the food becomes a menace to the health of the middle-aged. McCarrison considers that the continued use of foods poor in vitamins is responsible for a general derangement of the functions of the digestive tract. Its resistance to infection is thus lowered; the secretory and digestive functions are impaired; its powers of assimilation are reduced; the nervous and muscular mechanism controlling the movements of the stomach and bowels becomes ineffective. These conditions lead to such disorders as dyspepsia, dilatation of the stomach, gastric and duodenal ulcer, obstinate constipation, catarrhal conditions of the digestive tract, colitis, etc. McCarrison's conclusions are based upon many years' clinical experience and upon research work carried out at the Pasteur Institute of Southern India. Every aspect of the question, from the first departure from normal health, was studied in

[1] Quoted in *Contributions to Medical and Biological Research*, New York, 1919.

the laboratory upon animals. He observed the effect of a complete deficiency of individual vitamins and of partial deficiencies of all the vitamins. The progressive ill-health on these diets was investigated at each stage; post-mortem examinations of the organs, both in their gross appearance and in their microscopical changes, were made. A special study was made of the endocrine organs, that is, of the glands, such as the thyroid, pituitary, adrenals, etc., whose special secretions regulate and co-ordinate the functions of all parts of the body. On diets deficient in vitamins all the endocrine organs, except the suprarenals and the pituitary which enlarge, were found to atrophy. Administration of active preparations of these glands temporarily alleviated the effects of a bad diet. McCarrison concluded that dietetic deficiency led to endocrine insufficiency. Knowledge gained in the laboratory was applied to patients with striking success, and by simply changing the diet to food-stuffs rich in vitamins, he was able to produce cures in cases which had been previously unsuccessfully treated by other methods.

Quite independent observations made in America confirmed the accuracy of McCarrison's contention that many disorders, not hitherto associated with diet, may be traced to the habitual use of the wrong kinds of food. At the Annual Session of the American Medical Association, 1920, in the section of Diseases of Children, a subject for discussion was " The relation of food-dislikes acquired in childhood to the ills of middle life." Dr. Hilton Rice, in the opening paper, said the results of defective nutrition are not often immediately perceptible, but are cumulative in effect. With few exceptions, all healthy adults eat a variety of foods. Many children left to eat what they like turn to carbohydrates and form dislikes for essential foods, particularly for milk, eggs, fresh meat and green vegetables. Older children often show mild or pronounced symptoms of malnutrition for no other reason than that they have acquired

dislikes for essential foods. Many middle-aged sufferers from disturbances of metabolism have food dislikes that date back to childhood, and these individuals have always been anæmic and constipated. Deficient diet is the underlying foundation of more varied and mysterious ills than any single causal agent in the whole range of pathology. In the long-continued partial absence of essential food elements Dr. Hilton Rice saw the explanation of many of the disorders of middle life, such as gastric and duodenal ulcer, Bright's disease, hypertension, visceral ptosis, etc.

Other doctors gave further particulars:—

A dietetic study of school-children showed that many in the lower grades had no milk. In a group of 2000 children only 5 per cent. ate green vegetables. Children of ten and eleven used condiments and disliked essential foods. In Alabama the children ate chiefly bread and syrup; candy and ice-creams were eaten largely between meals; most of them disliked green vegetables.

Many tubercular patients had been observed to dislike milk and eggs and to refuse meat; defective diet and a lack of dietetic training were considered important factors in relation to tuberculosis.

Some food dislikes are caused by anaphylaxis, that is, a hypersensitiveness to certain proteins, such as the proteins of milk or egg, so that the individual cannot tolerate these foods; such cases are fortunately rare.

Defective nutrition in childhood was found to be the cause of rejection of two-fifths of the recruits for the British Army during the Boer War. The Provision of Meals Act, 1906, was therefore passed. Under this Act 29,560,316 meals were served in 1914; the number fell to 6,503,140 in 1918 on account of higher wages and allowances to soldiers' families during the war. Ninety per cent. of these meals were served free. In America the provision of free meals was abandoned, except in special cases, as it was found that free meals merely led

to a reduction in the home food-supply; 90 per cent. of the school meals are sold at cost price.

The institution of nutrition clinics in some American schools has been a great success. Children, not up to the standards of weight in relation to age and height, or otherwise showing signs of malnutrition, were given instruction in a special class as to the kinds of food to be eaten or avoided; they were also taught how to take care of their bodies. The homes were visited and the parents similarly instructed. Fifty-seven per cent. of these children gained weight at 1·7 times the average rate and 22 per cent. at about the normal rate; the remainder had more than one reason for failure. The children took a keen interest in their increasing size and strength and the good results were obtained under most adverse conditions.

CHAPTER XII

ERRORS IN THE SELECTION OF FOOD

THE principles underlying the choice of proper food have long been known, but not always followed. In 1772 Dr. William Cadogan, in a *Dissertation on the Gout; addressed to all invalids*, stated these principles concisely: "We ought to learn to balance the mixture (*i. e.* of animal and vegetable food-stuffs) with due proportion to prevent the diseases that are peculiar to the predominancy of either." He protested against the overcooking of meat, and declared that "the things we feed upon ought all to be in a perishable state or they will never furnish the materials of good blood, and whatsoever is hardened or seasoned so as to keep long ought never to be eaten at all. . . . Bread, so far from being the wholesome thing we imagine, is unwholesome, the bread of London particularly so, partly by being robbed of its bran and by having in it, besides its usual ferment, a great quantity of sour alum, most absurdly added to make it unnaturally white." Alum for whitening bread is seldom used since the passing of the Sale of Foods and Drugs Act, 1875, but the preference for white flour and refined cereal preparations continues. Millers should be encouraged to retain in the flour the valuable outer layers of the grain, which contain A- and B-vitamins, good protein and salts. In Denmark during the period when war bread was in use and white flour unobtainable, the general standard of health was greatly improved (p. 115).

There is nothing actively harmful in food-stuffs devoid of vitamins; they may supply economical fuel, and in many cases are a source of good protein. If a considerable portion of the diet is composed of such food-

stuffs, the absence of vitamins must be compensated for by the inclusion of substances especially rich in the missing factors, such as butter or cod-liver oil to supply A-; "marmite" to supply B-; orange-juice, lemon, cabbage, etc., C-factor.

Numerous preparations on the market are advertised to contain all the vitamins, but few potted preparations are likely to contain more than two. *The necessary vitamins are best and most cheaply supplied by fresh natural foodstuffs.* Information of the vitamin value of different foods is given in the tables in the Appendix.

Instinct is often believed to be a guide to the choice of food. It may serve amidst natural surroundings, but under the conditions of modern civilisation it is not proof against such temptations as are offered by cakes, chocolates, sweets, pickles and delectable dainties preserved in tins and glasses. Brown wholemeal bread is not generally liked and no instinctive need is felt for green vegetables and salads.

The provision of good food is not in itself sufficient. Every individual must eat his share of each kind of food. This obvious point has often been overlooked, but its importance was emphasised by both Goldberger and Vedder. Again and again a deficiency disease has appeared unexpectedly amongst people on an apparently adequate ration, and it has been said that in this instance the outbreak could not possibly be attributed to the food, and some other cause has been blamed. A detailed investigation made it clear that the food, though considered good, really consisted of food-stuffs lacking in one or more vitamins; or good food was provided and not eaten; or it was unevenly distributed. It frequently happens that one member of a household, or several members of a larger community, invariably reject certain items of food which are essential for health.

In the matter of food there is a tendency to lock the stable door after the steed is stolen. The invalid is

ordered nourishing food, which if taken earlier might have prevented the illness. The food of the convalescent consists of milk, eggs, fresh meat sometimes *raw*, chicken, fish, eggs, butter, fruits and vegetables; these are all foods rich in vitamins and good protein. If it is worth while to get well, it is surely better worth while to keep well. It is therefore necessary to consider how an insufficiency of vitamins and good protein most commonly arises, and the simplest means for remedying a defective diet. The accessory factors, generally speaking, are very unstable to temperature and other influences; they are very unevenly distributed in the various food-stuffs; a sufficient quantity of each must be consumed every day. The peculiarities of the individual vitamins and their distribution must always be borne in mind in choosing a diet and the least destructive methods of cooking employed.

The Supply of A-Vitamin in the Food.

Rickets in infants and young children is associated with a diet poor in A-factor and it is cured by cod-liver oil, the food richest in this vitamin. Infants are dependent on milk for their supply of A-factor. Deficiency arises from several causes: from the use of cow's milk, or of full-cream condensed or dried milks over-diluted with water; from machine-skimmed condensed milk; from patent foods consisting largely of prepared starch and made up with insufficient milk.

The milk of cows at grass contains more A-factor than the milk of the same cows on their winter food. Milk in winter, though richer in cream, is poorer in A-factor (see p. 62). The creaminess of milk is no guide to its antirachitic value. At certain times of the year a child receiving fresh whole cow's milk may for this reason only be getting a small amount of this vitamin, and hence the prevalence of rickets after the winter months. Breast-feeding is no protection against rickets if the mother's food is poor in A-factor.

The weaned child receives this vitamin from a mixed diet which ought to contain milk, meat, eggs, butter and vegetables in addition to cereal food. Amongst the poorer classes little of these expensive foods can be purchased, and the only food which contains A-factor in common use is milk. No definite daily quantity of milk can be fixed as a safety limit, for the value of milk in this vitamin is so variable, but as much as two pints daily may be necessary. In some cases the good mixed food of the family may not be suitably distributed amongst the members. Children are supposed to be sufficiently nourished if they have bread and jam and plenty of puddings with little meat or butter. It is unfortunately the custom to give to the father or wage-earner the best food, whereas his requirements for heavy manual work are actually better satisfied by the high energy value of bread, jam and margarine. The child needs the wherewithal to grow, that is protein and vitamins in addition to Calories.

Actual destitution only accounts for a small proportion of these poor diets, they are more often caused by the diversion of funds to various amusements and drink.

Rickets amongst the children of the more prosperous classes can generally be attributed to a misapprehension of the most suitable kind of food for young children. Sometimes fatty food is given in excess, causing digestive disturbance and imperfect assimilation of the A-vitamin. More often mothers and nurses are over-fussy about the child's food. "Rich" foods, that is fatty foods, are rigorously restricted; meat is considered "too stimulating" or "too indigestible." Egg and meat, both valuable sources of A-factor, are not both allowed on the same day; the number of eggs may be limited to one or two a week, as they are thought to be "so binding." Butter and jam must not be eaten on the same piece of bread and the child chooses jam. White fish, containing no vitamins, is highly esteemed as a food for little children, but the fatty fishes, rich in A-vitamin, such

as herring and mackerel, are forbidden. Fish is only allowed if boiled or steamed, and not fried in fat and dipped in egg and breadcrumbs as the child prefers it. Bacon fat, sometimes lacking in A-vitamin, is, curiously enough, sanctioned in most nurseries. Thus many natural sources of A-factor in the child's food are carefully eliminated, and the amount of milk, butter, or cream taken may not be sufficient to compensate for a general lack of A-vitamin in the rest of the food. Diets which are restricted in fat and protein make up their energy value with a large amount of carbohydrate. The child fattens upon the starchy food and is considered to be fine and well-nourished. If fretful, sweets are often given as a quietus. The desire for sweets and starchy food becomes habitual and good food may be refused. The child begins to ail, not necessarily from well-marked rickets, but possibly from some infection, such as bronchitis, due to lowered resistance. The fat child, according to nursery lore, is generally "chesty"; it is, like the laboratory animals on a similar diet, prone to lung affections. The doctor is called in and prescribes cod-liver oil. This is a fine example of human inconsistency, one hand gives what the other has taken away.

The requirements of the adult for this vitamin are not so great. If their food contains some sources of A-factor, such as eggs, herring, meat, milk or brown bread, they can safely use vegetable margarine instead of butter. On a diet very deficient in this vitamin adults may suffer from a bone disease (see p. 87), but a less complete deficiency of this vitamin usually manifests itself by lowered resistance to infection, particularly of the chest.

The Supply of the Antiscorbutic or C-Vitamin in the Food.

In the United States and in the British Isles the potato is the salvation of the working classes from scurvy. More than once a failure of the potato crop has led to an

outbreak of scurvy. In Ireland, in 1847, the year of the great famine, there was scurvy in all the large towns and cities. Dr. Curran, in the *Dublin Medical Journal* of that year, mentioned that the diet in four-fifths of the cases had been restricted to bread and tea or coffee. A failure of the potato crop in 1916 was followed by outbreaks of scurvy in Glasgow, Manchester and Newcastle, and there were several epidemics in the United States. This dependence on the potato as an antiscorbutic implies that a large number of people, although not in actual danger of contracting scurvy, yet are not taking sufficient antiscorbutic food-stuffs to keep themselves in good health. The general margin of safety during the winter months is thus dangerously low. Professor Hopkins [1] traced a period of ill-health amongst boys in a preparatory school to a lack of fresh fruit and vegetables during the winter months. It is this sub-minimal supply of any vitamin which undermines the health.

Green vegetables, salads and fruits are the other common antiscorbutics. Salads and fruits in the winter are scarce and dear and consequently omitted. Oranges are cheap during the winter and spring, and are the best antiscorbutic obtainable. Many people are content without any fruit or green vegetables and prefer pickles and other condiments.

The antiscorbutic value of green vegetables is often spoiled by the methods of cooking (p. 66). It may be destroyed by cooking with soda to improve the colour. Long slow cooking as in stewing, or in hay-box or other self-cookers, involves keeping the meat and vegetables at a temperature just below boiling point for some hours, and is destructive of the antiscorbutic property. Scurvy broke out in a camp in Scotland in the spring of 1917 and 82 men were affected. Potatoes were scarce at that time, but a good ration of fresh meat and swede turnips was issued daily and should have afforded protection. Professor Leonard Hill, who investigated this outbreak,

[1] In the Huxley Lecture, 1921.

discovered that the meat and vegetables were always stewed together for about five hours, a period sufficient to destroy the antiscorbutic factor. Miss Chick has recorded 40 cases of scurvy among children at a tubercular clinic in Vienna in 1920. On investigation, the good vegetable ration provided was found to be spoiled by the method of cooking, which involved heating twice; the vegetables were first boiled in water and then fried in fat. The common practice in this country of boiling more potatoes than are required and then re-heating by mashing or frying is a mistake.

Vegetables and fruit are not all of the same antiscorbutic value (see table, p. 61). Oranges, swede turnips, cabbages and spinach are excellent; apples, grapes, cauliflowers and carrots are of little value. The substitution of rice or dried vegetables, or of dried prunes, figs and dates for fresh fruit and vegetables does not answer the purpose. Dried peas, beans and unsplit lentils can be turned into true substitutes for fresh green vegetables by germination. The seeds are soaked in cold water for twenty-four hours, the water drained away and the seeds kept on a moist cloth exposed to the air till they begin to sprout. The flavour of peas and lentils is greatly improved by germination, and much less cooking is needed to soften them; germinated beans are not palatable. Whole lentils of various kinds are much used in India but difficult to obtain in this country.

Some people complain that vegetables cause indigestion, but this may be because they are not eaten often enough. Kramer (1720) cured patients of scurvy by the expressed juice of scurvy grasses and cresses, and recorded that after each dose they suffered from " prodigious belchings and wind." Those unaccustomed to the use of fresh fruits and vegetables may feel temporary inconvenience on first taking them. Fruit or swede juice given to infants may cause flatulence or have a laxative action, but the child soon accustoms itself to the new food and its digestive powers are

strengthened. Cases of digestive derangement are commonly treated by withholding fruit and vegetables; this prohibition may augment the trouble. Nine French children repatriated from regions occupied by Germany, as recorded by Weill and Dufourt, were suffering from inflammation of the gums and bowels and also from dysentery. Fruit and vegetables were withheld in the belief that they would aggravate the bowel symptoms. The children eventually developed scurvy. On giving an antiscorbutic diet they were all cured of scurvy and the bowel symptoms disappeared also. From the cradle to the grave it is never safe to avoid all fresh food. Dr. William Young describes the case of an old lady of seventy-seven in New Zealand, who by doctor's orders ate no meat, fruit or vegetables on account of pain, vomiting and flatulence; cancer of the stomach was suspected. Boiled milk was her principal food. The patient began to have fits of nose-bleeding and suffered from general malaise; later typical scurvy developed. Fresh milk, raw meat juice and orange juice were ordered. The scurvy was cured, and after a short time all the distressing gastric symptoms were cured.

Fruit and vegetables should not be omitted from the diet on the plea of indigestion; their use, if persevered in, is likely to cure many digestive troubles.

Milk for the infant is the natural source of this vitamin and must be treated with care. Like vegetables, it loses value on heating; boiling for a short period is less destructive than keeping at a lower temperature for a longer period. The re-heating of milk completely destroys the C-factor. Many cases of scurvy in infants have been caused by the use of commercially pasteurised milk being re-heated once or more often in the home. The addition of alkali in any form to milk foods for infants should be avoided (see p. 67).

The diet of the nursing mother should contain fresh fruit and vegetables, since it has been shown that the antiscorbutic value of milk depends on the diet. Cows'

milk is richest in this vitamin when they are at grass. It is a common practice of maternity nurses to forbid the mother to eat green vegetables, as they are supposed to give the baby wind, and to forbid fruits because the acid juice is supposed to curdle the milk. The infant will thrive best if the mother eats some fruit and vegetables, and no amount of acid taken by the mouth can curdle the milk in the breast.

The Supply of the Antiberi-beri, or B-Vitamin, in the Food.

Commercial processes interfering with food-stuffs derived from seeds of cereals and legumes are the main causes leading to a shortage of B-factor. Most of the farinaceous foods in use in this country, white flour, rice, cornflour, sago, tapioca, pearl barley, pea-flour, oatmeal, split peas and lentils, do not contain the B-factor which is present in the whole grain or seeds. The amount of B-factor in the yeast used in bread-making is insufficient to compensate for the quantity removed by milling. Rowntree [1] has shown how largely bread, cakes and puddings figure in the diet of the labouring classes. These foods are the cheapest for supplying the energy requirements. The other food-stuffs in common use were potatoes, jam, cheese, tea, coffee and a little milk; none of these contain sufficient B-factor to compensate for the extensive use of white flour and other farinaceous foods. Amongst the more prosperous people a large amount of white farinaceous food is consumed, but in this case the shortage of B-factor is to a certain extent balanced by the larger quantities of eggs, fruit and vegetables which are eaten.

In this country cases of severe dyspepsia have been attributed by Dr. Simon Fraser to the consumption of white bread. The digestion returned to normal within a week after whole-meal bread was substituted for white

[1] *Poverty; A Study of Town Life.* By B. Seebohm Rowntree.

bread. The symptoms in these cases—pain and tenderness in the regions of the stomach, flatulence, very rapid pulse rate, loss of power over voluntary muscles, shortness of breath and giddiness—are identical with the early symptoms of beri-beri (p. 14).

The shortage of B-vitamin in the diet of all classes is not sufficient to produce beri-beri except in rare cases, but this continual shortage is probably responsible for most of the chronic constipation, appendicitis, colitis, stasis, gastric and duodenal ulcers from which the present generation suffers (see p. 118). The benefit of a "change of air" is very likely the effect of a change of food; more eggs, fruit and vegetables are generally eaten whilst on holiday.

There are several ways in which poverty of the diet in B-vitamin can be remedied. Wholemeal wheat, rye, barley, maize and oats can take the place of the denuded cereal preparations at present on the market. Some wholemeal bread is available, but white bread is preferred by most people Some kinds of brown bread are made from white flour with added bran, but contain no germ. The whole seeds of peas, beans and lentils are a valuable source of this vitamin. It is contained in most fruits and vegetables, and if eaten in large quantities they will supplement the deficiency of the cereals. Another alternative is to take each day some special food-stuff containing B-factor in great concentration so that it can make good for the absence of the vitamin in the diet as a whole. Autolysed yeast extract, commonly known as "Marmite," is such a food; it can be used for all the same purposes as meat extract.

Infants fed on whole cow's milk alone apparently receive sufficient B-factor, but milk is not rich in this vitamin. Experiments upon dogs, pigs and fowls carried out by Gibson and Concepcion showed fresh cow's milk to be very poor in this vitamin, and they recommended that in infant-feeding the milk diet should be supple-

mented as soon as possible; sterilised milk was not more deficient than the fresh milk.

Comparatively few babies receive whole cow's milk. It is usually diluted with water and supplemented by some highly milled farinaceous preparation, thus lessening the amount of B-factor, although more is probably required for the metabolism of the extra carbohydrate. Infantile beri-beri has not been described outside the Orient; the symptoms may be overlooked in isolated cases. Both in America and Germany some of the signs of infantile beri-beri, such as tachycardia (rapidity of the heart's action), enlargement of the heart to the right, and œdema have been associated with infantile scurvy. Hess has shown that this group of symptoms is relieved by giving extract of wheat germ (= B-factor), just as infantile beri-beri is cured by extracts of rice polishings. These cases really appear to be a mild form of infantile beri-beri, and the symptoms might have passed unnoticed if the presence of definite scurvy at the same time had not attracted attention to these cases. The occurrence of these symptoms indicates that in infant feeding the supply of B-factor is insufficient if the milk is diluted and white cereal preparations (wheat, barley, or cornflour) added. During the war, Dr. Aron called attention to the remarkable way in which infants thrived when white flour was scarce and their milk was thickened with a cereal preparation containing a large proportion of bran. It would be an excellent thing if all patent foods for infants contained the germ and bran of the grain in a finely divided form.

The condition of marasmus (wasting) in infants is responsible for many deaths. It may be associated with tuberculosis or syphilis, but in most cases is regarded as "a vice of nutrition." The particular fault in nutrition may be connected with the supply of B-factor. There may be too little in the food, for we have just seen how dangerously near the border-line of inefficiency the infant's

food may be. Some infants may have a greater need for this vitamin and fail on food which suffices to keep others in fair health.

Eddy and Roper (1917) in the United States gave additional B-factor in the form of a preparation of fresh lamb's pancreas (p. 66) to nine marasmic babies. Tested on rats the extract of pancreas was found to be rich in B-vitamin. The treatment produced growth in the babies at once; growth continued as long as the vitamin was given; after periods varying from 6 to 69 days, it was stopped and growth gradually ceased. A second period of treatment with vitamin preparation produced renewed growth, and at its end the infants were given whole milk and continued to progress. Starch was found in the stools during the marasmic period, but it disappeared soon after treatment. Fig. 24 is the growth chart of one infant.

This child had been breast-fed for the first month of its life and was afterwards given a mixture of one-third milk to two-thirds water, a mixture obviously very poor in all three vitamins by reason of its dilution. Later, the food consisted of milk over-diluted with barley-water and sugar. Marasmus developed and was not cured by the ordinary hospital treatment. The addition of the active preparation of B-vitamin immediately produced growth, as seen in the chart.

Another case had made no growth during 123 days' trial of other diets, but growth began at once with B-vitamin treatment. As soon as the children were able to take whole milk no additional vitamin was required.

Diluted milk thus needs to be supplemented with B-vitamin. The infants in this experiment received orange-juice, and apparently derived enough A-factor from the milk.

Byfield and Daniels successfully treated marasmic infants with large amounts of orange-juice. Infants who were stationary in weight on a diet of boiled milk and 15 c.c. of orange-juice daily began to grow when the

amount of orange-juice was increased to 45 c.c. daily. Growth ceased if the orange-juice was reduced to 15 c.c. again, as shown in the weight charts (Fig. 25).

Experiments with the same diet were carried out on rats; they did not grow if the B-vitamin was removed from the orange-juice by precipitation with fuller's-

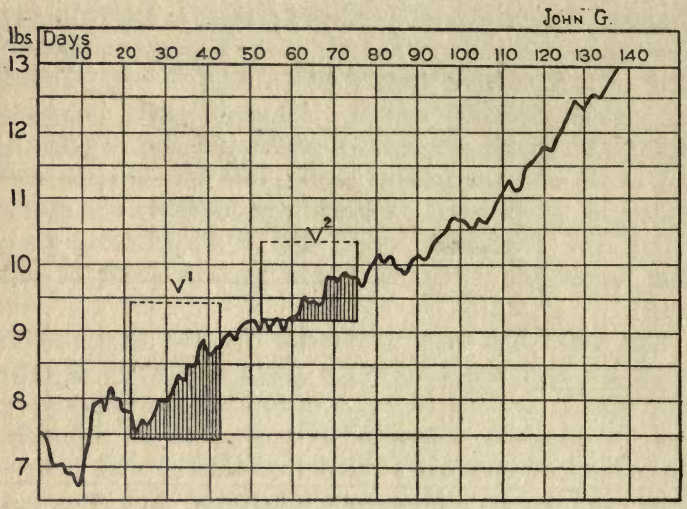

FIG. 24.—Weight Chart of Marasmic Infant showing Effect of Treatment with B-vitamin. The vitamin was given at periods marked V^1 and V^2 (Eddy and Roper).

Reproduced by kind permission from *Amer. J. Diseases of Children*, 1917, 14, 189.

earth reagent (see p. 65). In another experiment the C-factor in orange-juice was destroyed by alkali, but the rats continued to grow. It was therefore concluded that the growth in infants was stimulated by the B-factor supplied in the large amount of orange-juice. 15 c.c. of orange-juice supplied sufficient C-factor, but larger quantities are required if the juice is also to serve as an additional source of B-factor in the diet. The presence of B-vitamin in orange-juice has also been demonstrated by Osborne and Mendel.

Marasmic infants were treated with very large quantities of fruit-juice, up to 24 oz. per day, in addition to suitable pre-digested food, by Dr. Gladstone (London, 1916). Three parts of orange-juice to one part of apple-juice diluted with one-quarter water were used; when oranges were out of season they were replaced by the juice of

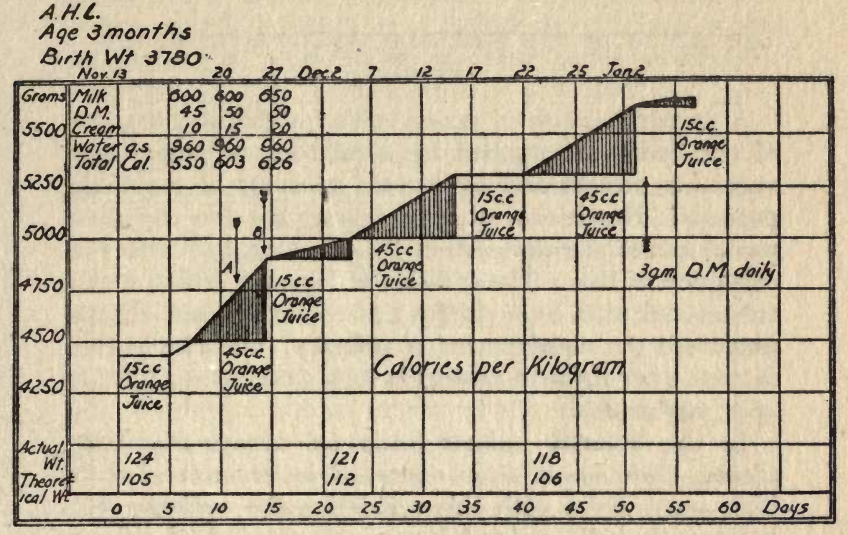

FIG. 25.—Weight Chart of Marasmic Infant showing Effect of Treatment with B-vitamin contained in large amounts of Orange Juice (Byfield and Daniels).

Reproduced by kind permission from *Amer. J. Diseases of Children*, 1920, **19**, 349.

strawberry, cherry, raspberry, banana and a little lemon-juice. The children gained in weight after a slight initial loss. It seems likely that B-factor was the active agent in this case also, as much more C-factor than necessary must have been given.

The requirement of infants in B-factor, or antiberi-beri vitamin, is a point which has not been sufficiently considered even by those who appreciate the necessity of an adequate supply of the antiscorbutic and antirachitic vitamins. There is some evidence to suggest that a

shortage of this factor in the diet may play a part in the development of rickets. The utilisation of good fats (*i. e.* of A-vitamin) in the food is to a certain extent dependent on an adequate supply of B-factor (p 58), and the amount of B-factor needed is larger than the quantity which the child receives if the milk is diluted.

The Supply of the Essential Amino Acids in the Food.

A proper mixture of amino acids for the maintenance of our bodies is supplied by a mixture of animal and vegetable protein and by certain mixtures of vegetable proteins. Nutritional disaster follows the too exclusive use of cereal proteins, especially of maize, but with the exception of rice. The addition of legumes, fruits, roots, tubers and nuts to a chiefly maize diet has not always prevented the development of pellagra; no cases of this disease occur if cereal protein is supplemented with meat, milk, egg or fish.

In this country animal foods are always available, though their use is often restricted on account of their high cost. Even with this restriction the ordinary diet is above the pellagra level, because the staple food, wheat, contains better protein than maize. Meat is usually taken with the Sunday dinner, eggs occasionally, and a little milk daily. The biological value of the protein may not in all cases be high enough to secure perfect health. Dr. Charles Mercier (1916) proved that diet is a factor in the causation of mental disease. Thirty-five patients had consulted him for the treatment of headache, sleeplessness, depression and mental confusion. Their food, in practically every case, had consisted of a very little meat and a great deal of bread, butter, cake and sugar; the small amount of meat was due in some cases to poverty, in others to faddiness. The dietetic history and the nervous symptoms corresponded to the early stages of pellagra. Mercier prescribed more meat and less sugar

and butter; in those cases in which his advice was followed rapid improvement took place.

Pellagra is always far more frequent among women; this is not due to a greater susceptibility, but simply to a difference in diet. Where the means are limited, the meat is mostly given to the man, even during the pregnancy and lactation of the woman. The woman's appetite is often spoiled by the heat of the fire and the smell of the food during its preparation; it is more easily affected by overwork, anxiety, bereavement or any other emotional influence.

Roberts (1920) published an account of twenty-five cases of pellagra in the United States, amongst his private patients, who developed the disease as a consequence of food faddiness. A wealthy widow, aged twenty-five, living in the country, for two years refused to eat eggs, meat, chickens, peas and beans, and ate only cereals, bacon, cabbage, spinach and biscuits. She developed pellagra and was cured by a proper diet. Another woman, also wealthy, would eat only a little fruit, maize cakes, or salad; wholesome food was refused. She lost 25 lbs. in weight and suffered from insomnia Acute pellagra developed and she died in two months. A third woman lived in the country, grew green vegetables and kept her own chickens and cows. Her house was burned and a brother killed in the war. The worry made her appetite irregular and peculiar; she desired chiefly fat pork, greens, bread and coffee, and disliked chicken, eggs and milk. Pellagra developed and was cured by proper dieting.

Another case suggests that many chronic invalids may be merely victims of their own diet fads and might be restored to health by a change of food. A young married woman from her childhood had many food dislikes; she never took milk, eggs, or vegetables, and meat only in the form of an occasional ham sandwich, but liked bread, cakes, syrup, sweets and butter. She had a sore mouth for several years and finally developed severe pellagra. On treatment with proper food she gained 54 lbs. and weighed

22 lbs. more than she had ever done before. She now eats regularly and freely of all the foods that she had previously refused. This woman had everything that money could give, and was reared in the same environment as her healthy sister and athletic brother, but differed from them in her peculiar and unexplained repulsion towards ordinary wholesome food. The other cases were similar, and out of the twenty-five recorded by Roberts only four of them were men.

Pellagra has developed in patients put on a diet poor in animal protein to relieve asthma.

Tramps in this country, who have been living largely on bread, are said to suffer from an irritable condition of the skin which they call "bread itch." Possibly this may be a pellagrous rash, but alterations in the texture of the skin are sometimes associated with a scorbutic condition, and the diet was probably also lacking in the antiscorbutic factor.

APPENDIX

DISTRIBUTION OF THE VITAMINS IN FOODS

THE sign + denotes merely that the vitamin is present; + + + + that the vitamin is present in a relatively large amount; o indicates its absence; blanks are left for foods which have not been tested. The foods, unless expressly stated, were tested in the raw condition, and loss of antiscorbutic value during cooking must be allowed for. Many of these values are taken from the table in Report 38 of the Medical Research Committee.

	A-Factor.	B-Factor.	C-Factor.
Animal Foodstuffs.			
Meat: muscle, raw	+	+	+
,, cooked	+	+	less than +
,, salted and cooked			o
,, tinned		o	o
blood			
brain, raw	+	++	
heart, raw	++	++	
kidney, raw	++	+	
liver, raw	++	++	+
pancreas, raw	+	+++	
thymus, raw	o	+	
Commercial Extract of Meat	o	o	o
Gelatin	o	o	o
Milk: raw, whole	++	+	+
,, skimmed	o	+	+
,, pasteurised	++	+	less than +
,, sterilised	+	less than +	o
,, whole, condensed, sweetened	+	+	+
,, whole, condensed, unsweetened		o	
,, dried	+	+	sometimes +
,, colostrum	+++		
Cheese, whole milk	+		
,, skimmed milk	o		

	A-Factor.	B-Factor.	C-Factor.
Fish, white flesh	o	o	o
„ salmon, herring, mackerel	+	o	o
„ liver	++		
„ cod, soft roe	+		
„ turbot, hard roe	+	++	
Egg, yolk	++	++	o
„ white	o	o	o
Dried eggs	+	++	o
Animal Fats.			
Bacon fat	+variable	o	o
Beef fat (suet)	++	o	o
Butter	+++	o	o
Cod-liver oil	++++	o	o
Cream	++	o	o
Lard	o	o	o
Pig, fat round kidney	++	o	o
„ „ subcutaneous	+	o	o
Mutton fat	+	o	o
Oleo-margarine	++variable	o	o
Vegetable Oils.			
Almond	o	o	o
Coconut	o	o	o
Cotton-seed	less than+	o	o
Linseed	o	o	o
Maize	+	o	o
Olive	less than+	o	o
Palm kernel	sometimes+	o	o
Peanut	less than+	o	o
Sesame	o	o	o
Vegetable margarine=hydrogenated fat	o	o	o
Fruits.			
Apples		+	+
Bananas	+ ?	less than+	less than+
Blackberries			++
Cherries			
Cloudberries			++
Cranberries			
Currants, black, white and red			+
Damsons			
Dates, fresh			
Figs, fresh			
Gooseberries			+
Grape fruit	o	+	
Grapes		less than+	less than+
Greengages			
Lemons	o	+	++++
Lime-juice, preserved		+	o
Limes, fresh		+	++
Melons			

	A-Factor.	B-Factor.	C-Factor.
Mulberries			
Nectarines			
Oranges	less than+	+	++++
Peaches			
Pears		+	
Pineapple			
Plums		+	
Pomegranate			
Pumpkin			
Raspberries			++
Strawberries			++
Tomatoes	+	+	+++
Whortleberries			
Dried Fruits.			
Currants		o	
Dates		o	
Figs			
Prunes		++	
Raisins			
Sultanas			
Tomatoes		++	+
Vegetables.			
Artichoke, globe			
,, Jerusalem			
Asparagus			
Beans, green pods			
Beetroot		less than+	o
Brussels sprouts			
Cabbage, raw, green leaves	++	+	+++
,, ,, white leaves	o		
,, cooked, without soda for 20 min.	+	+	++
,, dried and cooked	+	+	less than+
Carrots	+	+	+
Cauliflower			+
Celery		+	
Cress			++
Cucumber			
Curly Kale			
Dandelion			++
Garlic			++
Horseradish			++
Kohl-rabi			++
Leek			
Lettuce	++	+	++
Marrow			++
Mushroom			
Mustard (and cress)			
Onion		++	++
Parsley			+++
Parsnip			+
Peas, green			

	A-Factor.	B-Factor.	C-Factor.
Potatoes raw. . . .	less than+	+	++
,, boiled . . .		+	+
,, peel . . .		+	
Seakale			
Spinach	++	+	++
Swede turnip . . .			+++
Sweet potato . . .			
Turnip, white . . .			
Watercress			++
Nuts.			
Almond	+	++	
Barcelona	+		
Brazil	+	++	
Butternuts	+		
Chestnut, Spanish . .		++	
Coconut		++	
,, milk . . .			++
Filbert		++	
Hazel			
Peanut (see under Legumes) .			
Pecan		++	
Pine kernel		++	
Walnut	+	++	
Legumes or Pulses.			
Beans, haricot, dry . .	o	++	o
,, ,, germinated .		++	++
,, soya, dry . . .	+	++	o
Lentils, dry, whole . .	+	++	o
,, germinated . .	+	++	++
Peanut (arachis, ground-nut or monkey-nut) . . .	+	++	o
Peas, dry	+	++	o
,, germinated . . .	+	++	++
Cereals and Farinaceous Food-stuffs.			
Barley, whole grain . .	o	++	o
,, sprouted . . .		++	++
,, pearl, or peeled . .	o	less than+	o
Maize, whole grain . .	+	++	o
,, meal, yellow . .	+	sometimes+	o
,, white cornflour . .	o	o	o
Millet, whole grain . .	+	++	o
Oat, whole grain . . .	+?	+	o
Oatmeal		less than+	o
Rice, whole grain . . .	+	++	o
,, polished . . .	o	o	o
,, "polishings" (germ + bran) . . .	+	++	
,, germ		+++	
Rye, whole grain . . .		++	
,, flour		++	

	A-Factor.	B-Factor.	C-Factor.
Wheat, whole grain	+	++	
„ germinated (= "frumenty")	+	++	++
„ germ	+	++	
„ white flour	o	o	o
„ „ „ +added bran	o	+	o
Wheat bread, wholemeal	+	++	o
„ „ white made with yeast and milk	less than+	less than+	o
Egg substitutes	o	o	o
Malt		sometimes+	
Pea-flour, kilned	o	o	o
Sago		o	o
Tapioca (manioc)		o	o
Miscellaneous.			
Beer, as now manufactured	o	o	o
Beer, "home-brewed"			+
Chocolate			
Cider, freshly made			+
Cocoa			
Coffee		+?	
Honey			
Jam			
Malt extract		sometimes+	
Pickles			
Sauerkraut			
Tea, black			o
„ fresh green China			+?
Yeast	o	++	o
„ extract, autolysed (="Marmite")	o	+++	o
Feeding Stuffs for Animals.			
Bran	o	++	o
Brewers' grains		o	
Cotton seed	+	+	o
Flax	+	+	o
Hemp seed	+	+	o
Oil-cakes	sometimes+		o
Millet	+	+	o
Sunflower seeds	+	+	o
Alfalfa (lucerne)	++	++	++
Clover	++	++	++
Grass	++	++	++
Hay, from immature grass		++	
„ „ mature grass		+	
Silage	+		o
Timothy	++	++	++

Common Food-stuffs containing all three Accessory Food Factors.

Food-stuff.	A-Factor (antirachitic)	B-Factor (antiberi-beri.)	C-Factor (antiscorbutic.)
Cabbage, fresh	++	+	+++
,, cooked	+	+	++
Potato	less than+	+	+
Pulses, germinated	+	++	++
Cereals, germinated	+	++	++
Liver	++	++	+
Cow's milk, whole raw	++	+	+
,, ,, dried	++	+	less than+
Lean meat	+	+	+
Carrots	+	+	+
Tomatoes	less than+	+	+++
Oranges	,, ,, +	+	+++

Food-stuffs Rich in A-Factor.

Butter	+++	Heart	++
Cod-liver oil	++++	Herring, mackerel	++
Cream	++	Cabbage, raw	++
Egg yolk	++	Lettuce	++
Wheat germ	++	Spinach	++
Beef fat	++	Wholemeal bread	+
Mutton fat	+	Carrots	+
Fish oil	++		
Liver	++		

Food-stuffs Rich in B-Factor.

Eggs, yolk	+++	Fish roe	++
Wheat germ	+++	Linseed and millet	++
Yeast, dried	+++	Dried pulses	++
,, autolysed "Marmite"	++++	Nuts	++
Liver, brain, pancreas	+++		

Food-stuffs Rich in C-Factor.

Cabbage, raw	+++	Germinated pulses	++
Lemon-juice	+++	Cabbage, boiled half hour	++
Orange-juice	+++	Potato, boiled half hour	+
Tomatoes	+++	Rhubarb	+or more
Swede-juice	+++		
Runner beans, pods	++		
Raspberries	++		
Salads	++		

Common Food-stuffs containing No Accessory Factors.

Fats and Oils.	*Meats, etc.*	*Cereals, etc.*
Lard.	Tinned meats.	White wheaten flour.
Olive oil	Fish, white.	,, cornflour.
Coconut-oil and -butter.	Cheese (skim milk).	Polished rice.
Linseed oil.	Meat extracts.	Pea flour, kilned.
Margarine from hardened vegetable oils.	Honey.	Custard powders.
Tea, coffee, chocolate, cocoa.	Jam.	Egg substitutes.
	Malt extracts.	Tapioca.
		Sago.

NOTES ON FOOD-STUFFS

Meat.

Meat contains a small and variable amount of all three vitamins. No distinction has as yet been made between the vitamin value of the flesh of different animals, such as pork, beef, etc. The small daily quantity of meat, some 4 to 8 ozs., which is usually eaten, may not supply enough of any one factor to compensate for an absence of vitamins in the rest of the diet.

Meat consumed in very large quantities protects from both beri-beri and scurvy. Krogh, who visited Greenland to study the metabolism of Eskimos, verified the report that they sometimes eat as much as 15 lbs. of meat in less than fourteen hours, and found that uric acid diseases, usually attributed to a meat diet, were very rare. The only vegetable foods eaten were whortle-berries during the autumn, which were swallowed like pills and passed through the intestine unchanged; young shoots of angelica were eaten as a delicacy in July; seaweeds were occasionally eaten; the half-digested débris of plants found in the stomach of the reindeer, was much liked but seldom obtainable. The chief or only food was boiled seal meat, liver and blubber. The *raw* liver of seals and the middle epidermal layers of certain whales are regarded by the Eskimos as a sure protection against scurvy, and their value has been fully confirmed by the medical officers of Greenland. Other instances of protection from scurvy by a diet almost entirely limited to meat are given on p. 34. Stefansson's experience in the Arctic regions was that boiled or roasted fresh bear meat relieved scurvy so slowly that it was debatable if

it had any curative effect, but its abundant use was a preventative.

The large amount of meat eaten by the Eskimos prevented beri-beri as well as scurvy, but small amounts of meat as the only source of B-factor do not prevent beri-beri.

Lean meat contains a considerable amount of fat not visible to the naked eye. The value of lean meat in A-factor may bear a direct relation to the percentage of fat contained in it, but so far a direct relation between the amount of fat and the amount of A-vitamin has not been established (cf. milk, p. 124). The fat of flesh (muscle) is not as rich in A-factor as the fat round the internal organs, *e. g.* kidney suet.

Tinned meats do not contain B- or C-vitamins, but are valuable as a cheap source of good protein.

Milk.

Milk, like meat and other animal tissues, contains good protein and a small amount of all the vitamins. It has been definitely proved that the milk of grass-fed cows is richer in A- and C-factors than the milk from cows artificially fed in the winter. Osborne and Mendel found that even the milk of grass-fed cows is poor in B-factor. Cows fed on swede turnips during the winter produce a milk containing a fair amount of C-factor. The value of milk in A-factor could be maintained at a good level during the winter if silage or the green tops of the swedes were more largely used as cattle food. Oil-cakes give a creamy milk poor in A-factor. Milk from suitably fed cows supplies a sufficient quantity of all three vitamins if it is the sole food. Milk usually forms only a small part of the diet, and then is not able to make good any vitamin deficiency in the rest of the food. The dilution of milk, as in the feeding of infants, reduces its vitamin value and may lead to stoppage of growth and the development of marasmus, scurvy, or rickets.

The vitamins in milk may be destroyed by the commercial and domestic processes to which it is subjected (p. 129). The vitamin content of dried and condensed milks cannot be adequately represented on the Table; every sample varies according to the value of the original milk and according to the processes of preparation. Milk dried quickly on hot rollers and protected from subsequent oxidation, retains some antiscorbutic value; if dried by spraying into a hot-air chamber the antiscorbutic value is much less. Sweetened condensed milk, prepared at a comparatively low temperature and relying on its high sugar content as a preservative, may retain some C-vitamin. As this factor is the most sensitive its survival is an indication that the A- and B-factors are not destroyed. Unsweetened condensed milks have to be sterilised during manufacture as they contain no preservative, and hence contain practically no trace of vitamins. The prolonged use of condensed unsweetened milks as the sole food during the treatment of cases of relapsing fever in a war hospital caused beri-beri. This disease appears before scurvy if both B- and C-factors are lacking.

Fish.

Beri-beri is very common amongst fisher-folk in the Orient, and fish frequently forms a considerable proportion of a diet which has led to the development of beri-beri. Fish, except the roes of fish, must therefore be considered as poor in B-factor. The flesh of fish certainly does not protect from scurvy, but the internal organs have not been tested for C-factor. The flesh of white fish contains little or no A-factor; fish oil expressed from fatty fish, such as herring or pilchard, contains this vitamin; the liver of fish contains it in very great concentration.

Eggs.

Birds are particularly sensitive to a shortage of B-factor and require an abundant supply of it in their food.

The yolk of birds' eggs is rich in this vitamin. Eggs have not been tested to see if their content of B-factor varies according to the supply of this vitamin in the birds' food. The yolk contains A-factor, but C-factor has not been detected. The white of the egg contains no vitamin. Dried eggs contain B-factor, but the amount of A-factor may be considerably diminished by the process of drying and by storage. Both yolk and white contain good protein. Egg-substitutes and custard powders are made from cereals, artificially coloured, and contain no vitamins.

Animal Fats.

The amount of A-factor contained in animal fats is dependent on the supply of this vitamin in the food. It must be particularly remembered that lard is devoid of A-factor. B- and C-factors are not contained in fats.

Vegetable Oils.

Freshly expressed vegetable oils contain a small amount of A-factor which may be destroyed by commercial refining and decolorising processes. Vegetable oils are generally prepared from the seeds of plants. The green tissues of the leaf or stem contain more A-factor than the oily seeds.

Fruits and Vegetables.

A very great number of fruits and vegetables have not yet been tested in the laboratory, but in herbals and other old records there is a store of information concerning the fruits and plants used in the cure and prevention of scurvy. Two plants, not now in common use on account of their unpleasant taste, were especially esteemed as antiscorbutics: English Scurvy-Grass, *Cochlearia officinalis*, a small cruciferous plant growing by the sea-shore in northern regions, and therefore easily accessible by sailors, the chief sufferers; Scottish Scurvy Grass, *Soldanella marina*, also known as sea-bindweed or sea-coal-wort. Other varieties of scurvy grass are found in

Denmark and Greenland. These herbs were prepared with wine or broths to disguise their acrimony. Onions, garlic, leeks, or eschalots were useful on board ship; one clove of garlic a day was considered sufficient to prevent scurvy. The cloudberry, little known in this country, as it is only found on mountains in the north of Scotland, is at the present day a valuable antiscorbutic in parts of Norway. Holst and Fröhlich have shown that its anti-scorbutic value is not entirely destroyed by the method used for preserving it with sugar. The cloudberry was referred to by John Peachey as the Cloudberry, Knot, or Knoutberry in his *Compleat Herbal* (1694): "'Tis said that in Norway they have so great an opinion of the Virtue of the Knotberry for curing the Scurvy that they remove their Scorbutick People to a neighbouring Island, and there they are forced to abide till they recover their Health, and having no other Provision allowed them, they feed on these Berries whereby they are infallibly cured in a few days." Of the bramble, Peachey records "that it is recommended for the Scurvy and not without Reason, for in Quality and Figure it resembles the Cloudberry, and therefore we need not charge Children so strictly not to eat them." As other valuable antiscorbutics this *Herbal* also mentions the orange, all kinds of cresses, the horse-radish, raw turnips and the growing tips of the fir tree (*Abies*). In the treatment of scurvy in the great Irish famine, Curran found "grapes, only useful when very sour"; gooseberry fool and the expressed juice of crab apples cured the disease, and eating a single rhubarb tart produced a "most decided amelioration in one gentleman."

Stefansson was told by miners in northern regions that three average-sized *raw* potatoes would definitely turn the tide in scurvy that had not reached an acute stage.

Green leaves contain all three vitamins, but are richer in A- and C- than in B-factor.

Salads are of course richer in C-factor than cooked vegetables; bleached leaves are lacking in A-factor,

therefore the practice of blanching salads is not to be recommended.

The vitamins of fresh dates do not appear to have been investigated, but it is reported by Dr. Moody that on the desert island of Henjam in the Persian Gulf the Persian coolies and their children live chiefly on dates, rice and fish, and do not suffer from beri-beri or scurvy; among the Indians employed on the island, receiving more liberal rations but no dates, there was one case of beri-beri and three of scurvy.

All the fruits which have so far been examined, except the banana and grape, are found to contain an appreciable amount of B-factor, but are relatively richer in C- than in B-vitamin. Few fruits have been tested for A-factor, but oranges, bananas and tomatoes contain a little.

The origin of the mistaken belief in preserved lime-juice as an antiscorbutic is explained by Mrs. Henderson Smith. The lime-juice, as first used in the Navy, was made from *Citrus medica*, that is the *sweet* lime or lemon from Spain. In 1860 there was a great development of the cultivation of limes in the West Indies, but these were *Citrus medica, var. acida*, sour limes. To encourage Colonial enterprise, and also because it was believed that antiscorbutic properties were associated with the degree of acidity, the sour limes took the place of the sweet lime or lemon for naval use. The juice of the fresh sour lime has antiscorbutic value, but it is not nearly as good as the lemon. Lime-juice deteriorates very rapidly on preserving, and preserved lime-juice has failed repeatedly to prevent or cure scurvy.

The antiscorbutic value of tinned fruits and vegetables is uncertain; it depends largely on the preserving process, and certain juices are more resistant to heat than others. The juice of tinned tomatoes was found by Hess to prevent scurvy in infants; it does not follow from this observation that all brands of tinned tomatoes are equally good. Tinned pineapple was considered in Mesopotamia to accelerate the healing of wounds in men in a prescorbutic

condition (p. 40). Slight benefit was derived from the use of tinned fruits (kind not stated) in the treatment of scurvy (p. 42). A diet composed almost entirely of tinned fruits and vegetables, including tinned baked beans, and of tinned meat and tinned milk, did not prevent either scurvy or beri-beri amongst railway employees in the Amazon basin.

Nuts, Legumes and Cereals.

Seeds of all kinds contain B-factor in large amounts in the germ and outer layers. The germ of cereals contains A-factor. C-factor is not present until the seeds are germinated. It is of the greatest importance that all seeds used for food should not have the B-vitamin removed by milling or decortication. Oatmeal has a legendary value as a preventive of beri-beri which is scarcely justified by facts. At one time beri-beri was common on ships with Scottish crews using much oatmeal. Laboratory experience with young chicks also showed a deficiency of B-factor in oatmeal. The absence of this vitamin in white bread is well known; even the addition of yeast and milk to the bread make no appreciable increment of B-factor.

Beer and Cider.

Beer as now used in this country has no vitamin value. Beer newly brewed from freshly germinated barley (sweet-wort) was reputed to be a very useful antiscorbutic if drunk in large quantities. Captain Cook, Sir Gilbert Blane and other experienced observers all testified to its value, which was further increased by the inclusion of the green buds of the fir trees in the making of spruce beer.

The winter diet of some of the natives of South Africa contains no antiscorbutic food-stuff. Protection from scurvy is afforded by large quantities, three gallons per man per day, of Kaffir beer made from freshly germinated millet. Scurvy broke out in 1918 amongst the South African Native Labour Corps in France. Their diet in

France was better than they were accustomed to at home, as it contained 9 to 16 ozs. of frozen or preserved meat daily and a small quantity of fresh vegetables, but the beer supplied was made from *ungerminated* maize and millet. The Kaffir or Basuto beer used in South Africa is called "leting"; it is made freshly each day from Kaffir corn germinated till the sprouts are half an inch long, dried and ground to a fine meal (malt) which is stirred up with boiling water; fermentation is started by adding the dregs of a previous brew. The beer is drunk next day while still visibly fermenting.

It is a very similar preparation to the sweetwort formerly made in England and not only prevents but cures scurvy. If freshly brewed beer of this kind were in common use in this country, beer-drinking would be an act of virtue.

The antiscorbutic value of Kaffir beer has been disputed, but the divergence of opinion is due to differences in the method of preparation; in some districts instead of merely stirring up the malt with hot water the mixture is boiled for two hours, a period long enough to destroy C-vitamin.

Large quantities of *freshly-made* cider will also prevent scurvy, and Lind showed that it had a slightly beneficial effect in the treatment of scurvy (p. 32).

Coffee.

Chocolate, cocoa and coffee as seed products are possible sources of B-vitamin, but only one attempt to test their value in this respect has so far been recorded; coffee was considered to have a slightly beneficial effect upon polyneuritic pigeons. The quantity in which these beverages are usually consumed and their method of preparation rule them out of consideration as a source of B-factor.

Tea.

The dry black tea in common use, extracted with hot water, is not likely to yield an appreciable amount of any

vitamin. It is of interest to find a record that there was less scurvy on the return voyages from the East in the old days because green China tea was purchased privately by the sailors for use on the homeward voyage. In one voyage the only two victims of scurvy were two sailors who had not provided themselves with tea; the others who drank the tea were free from scurvy; there was supposed to be no other difference in the rations.

Jam.

Holst and Fröhlich found that cloudberries and raspberries conserved by heating for a short time with sugar retained considerable antiscorbutic power. The use of marmalades of oranges and other fruits by the Spanish sailors in the seventeenth century failed to protect them from scurvy. Jams may contain a little B-factor but have not been tested; jams formed part of the Army ration which led to beri-beri during the war.

Yeast.

Autolysed extract of yeast ("Marmite") is the most convenient form for administering a concentrated amount of B-vitamin. Babies take it greedily. No ill effects have been observed to follow its use in large amounts.

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